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NIEHS: Future Directions

- Scientific vision
- Directions for growth
- Strategic planning

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NIEHS: Budgetary Considerations

Total NIEHS budget - 2005	**$724.3 million**
– DERT	$393.1 (54%)
– DIR	$110.6 (15%)
– National Toxicology Prog	$109.3 (15%)
– Campus operations	$76.4 (11%)
– Administration	$34.9 (5%)

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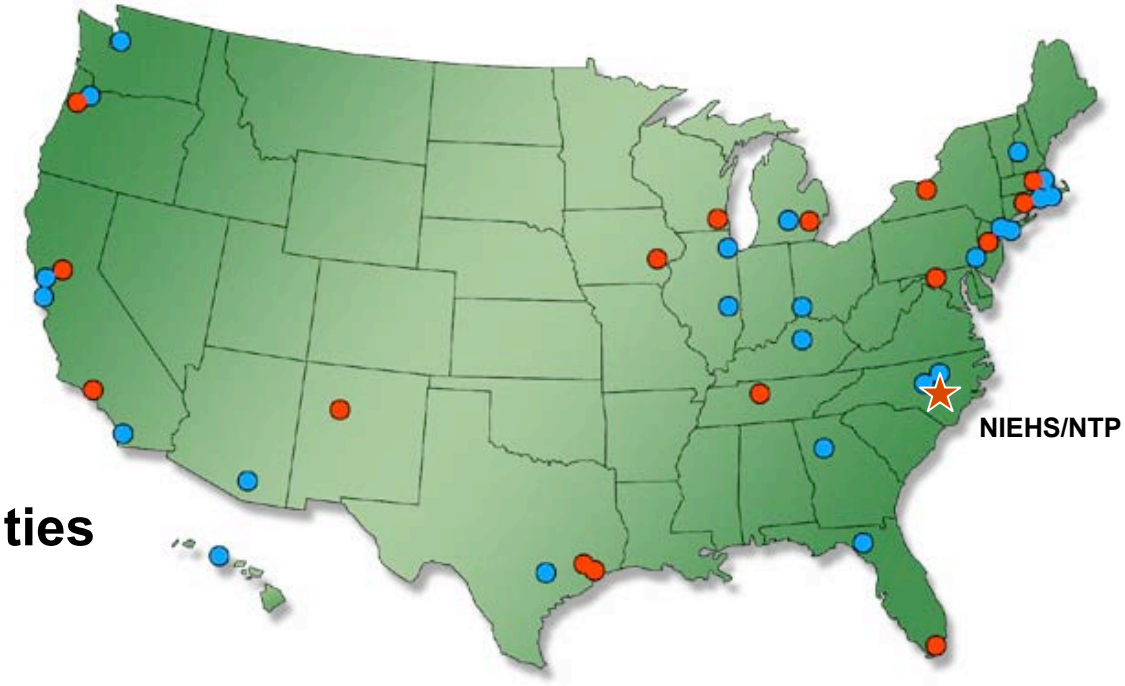
NIEHS Research Centers

- 26 Core Research Centers
- 16 Superfund Centers
- 11 Children's Centers
- 4 Breast Cancer Centers
- 3 Parkinson's Centers
- 3 Centers for Population Health and Health Disparities



NIEHS Research Centers in 2004: $72.2 million (23.3% DERT)

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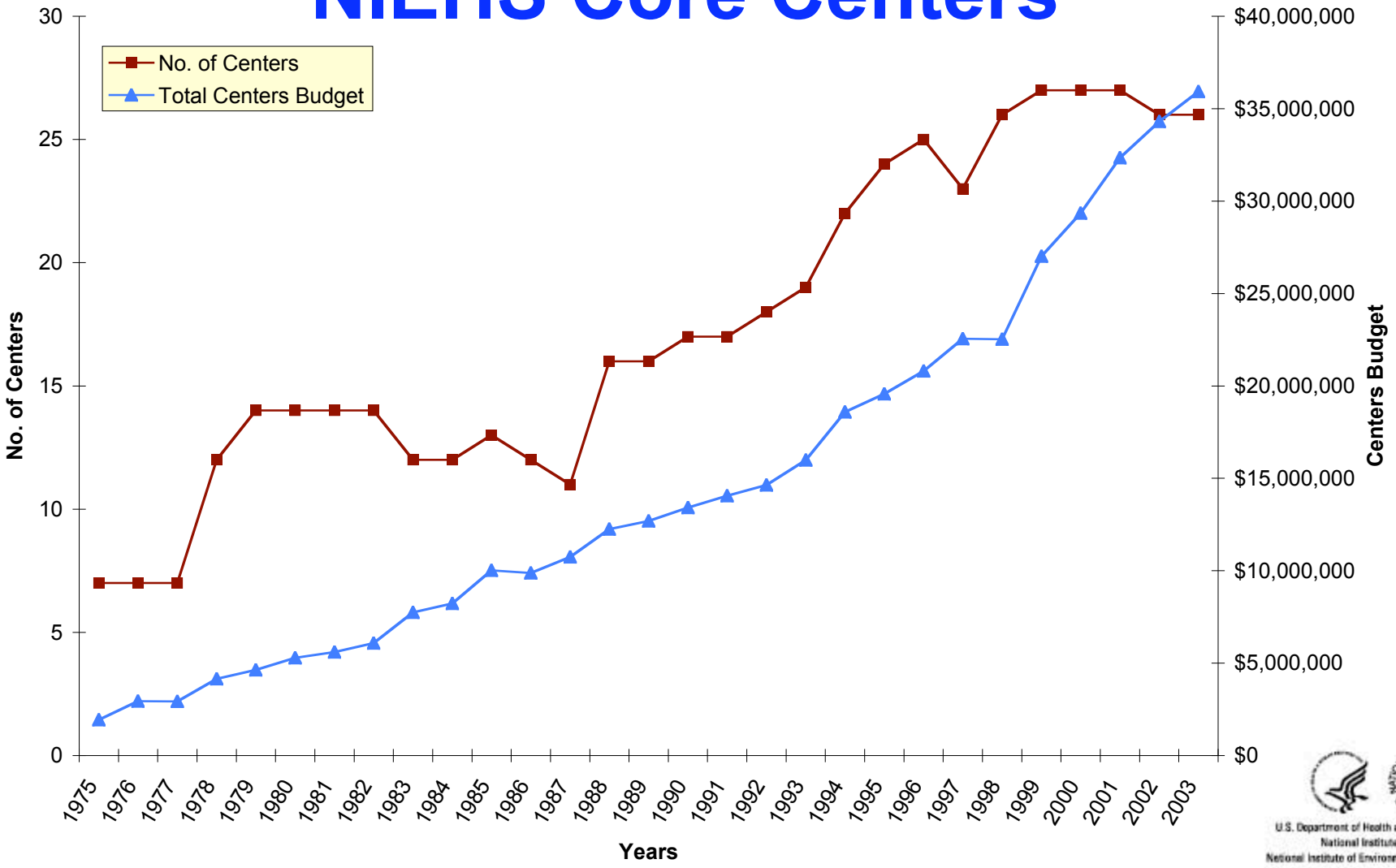
NIEHS Core Centers



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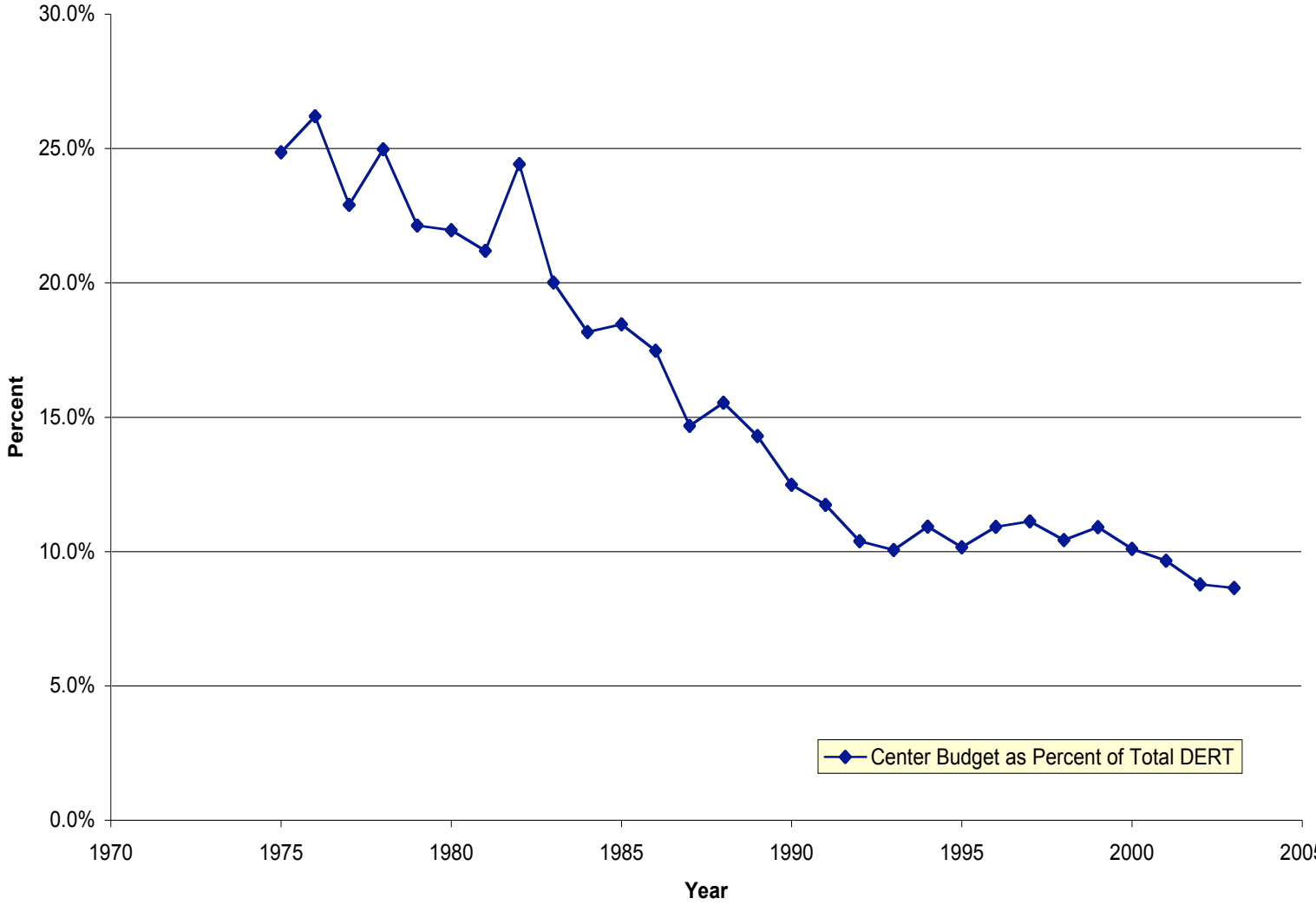
NIEHS Core Centers as % of DERT



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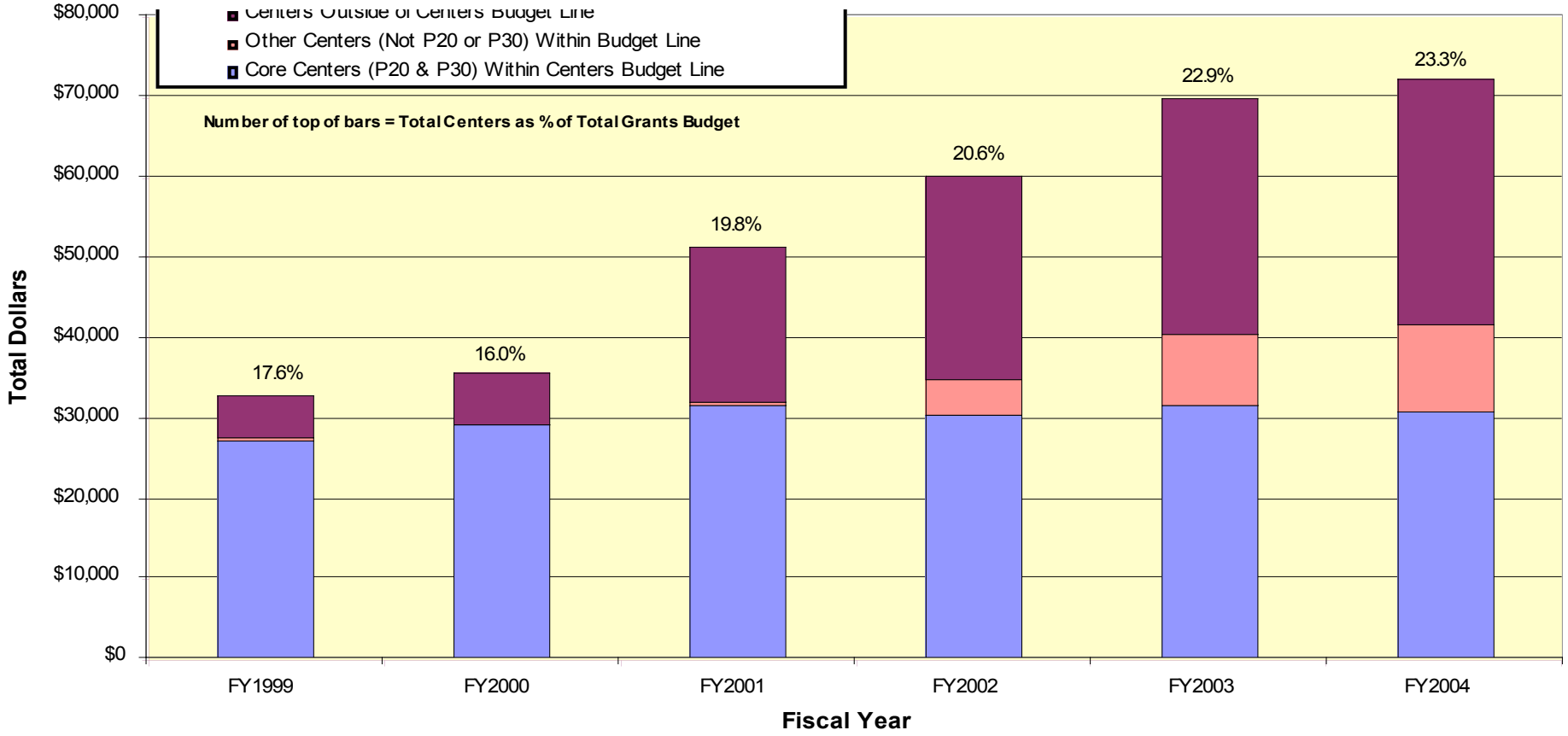
All NIEHS Centers as % of DERT



Centers Within Budget Line include P20 & P30 Core, G12 Minority, M01 Clinical, P50 Specialized, P51 Primate, U42 Animal, and U54 Specialized Centers
Centers Outside of Budget Line include P01 Children's and Botanical, U01 Mouse and Breast Cancer, and U19 Toxicogenomics Centers

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Vision for NIEHS

Use environmental sciences to understand human disease and improve human health

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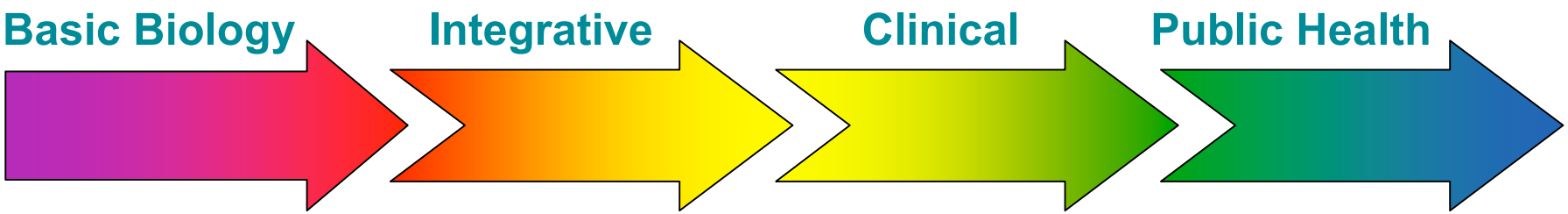
NIEHS Research Accomplishments



- AH receptor
- Endocrine disruptors
- Cell signaling
- Oxidant stress
- Metal biology
- DNA repair/mutagenesis
- Metabolism
- Development
- Gene regulation

- Air pollution and mortality
- Air pollution and lung development
- Lead and IQ
- Arsenic and cancer
- Aflatoxin and liver cancer
- Community outreach

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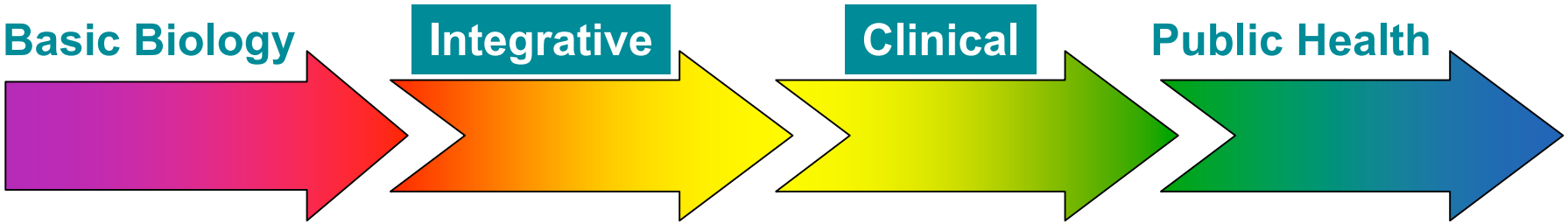
NIEHS Research Accomplishments



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Vision for NIEHS

Use environmental sciences to understand human disease and improve human health

Strategic Plan

- Scientific orientation
- Infrastructure
- Workforce

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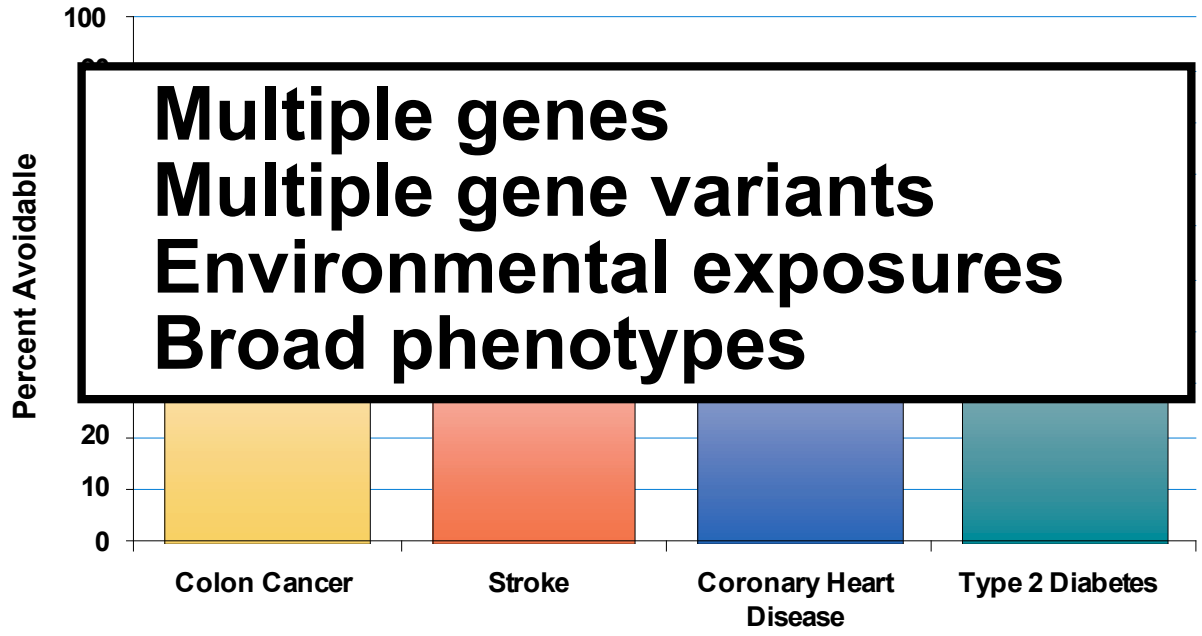
Scientific Orientation: Emphasis on Complex Human Diseases



- 70-90% of the major diseases in the USA are caused by reversible behaviors and exposures
- Single gene mutations are the major cause of cancers and CVD in < 5% of the cases

Willett. *Science* 2002; 296:695

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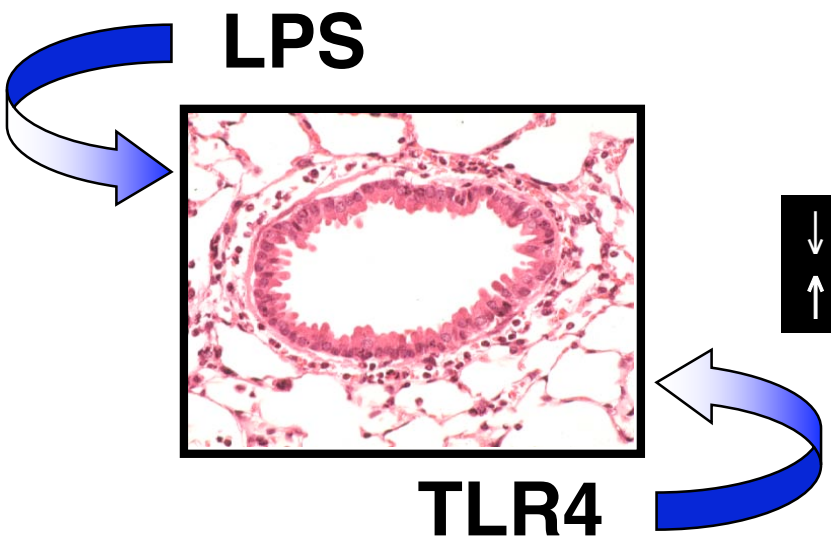
Exposures Can Simplify Complex Diseases

Exposures Can Simplify Complex Diseases

Asthma → House Dust Mite → Biological Phenotype



↓ LPS asthma and atherosclerosis
↑ GN sepsis and RSV bronchiolitis

Arbour. *Nature Genetics* 2000; 25:187

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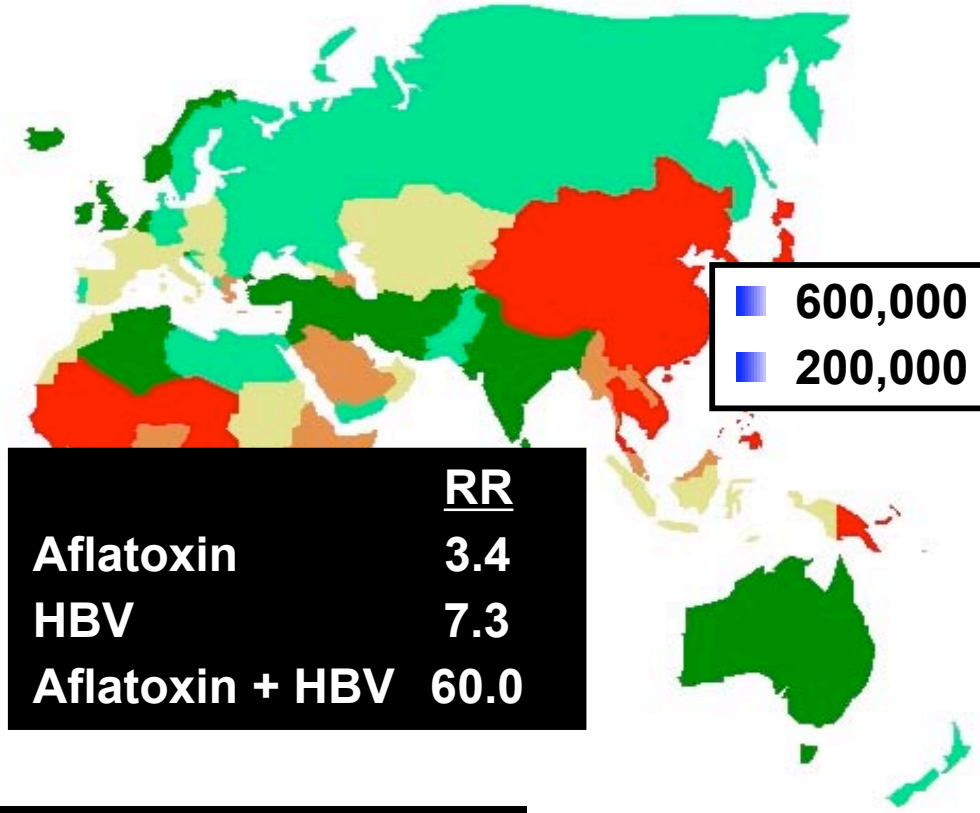
Scientific Orientation: Global Environmental Health



600,000 new cases
200,000 deaths

	RR
Aflatoxin	3.4
HBV	7.3
Aflatoxin + HBV	60.0

Hepatocellular Carcinoma

< 3.2 < 5.4 < 10.8 < 20.1 < 48.9

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Scientific Orientation: Natural Disasters

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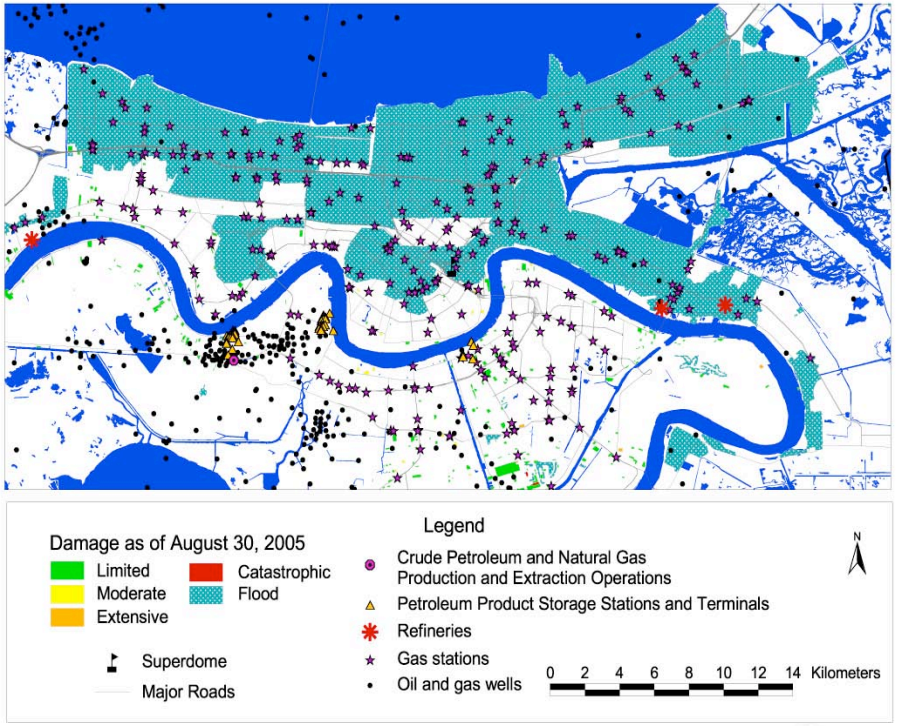
NIEHS Response to Hurricanes Katrina and Rita

- Support NIH medical relief
- Support CDC field public health teams
- Provide veterinary support
- Establish the Katrina website
- Geographic Information System (GIS) Maps
- Safety training for hurricane responders (WETP)
- Cooperative research with CDC and EPA
- Extramural research opportunities

www-apps.niehs.nih.gov/katrina/



Oil refineries in New Orleans area

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CommunityDispatch.com

Community News and Information
September 29, 2005

FEMA ANNOUNCEMENTS

Update and Health Issues Related to Mold, Mildew

Newsday.com
September 29, 2005

Mold a risk in Gulf area

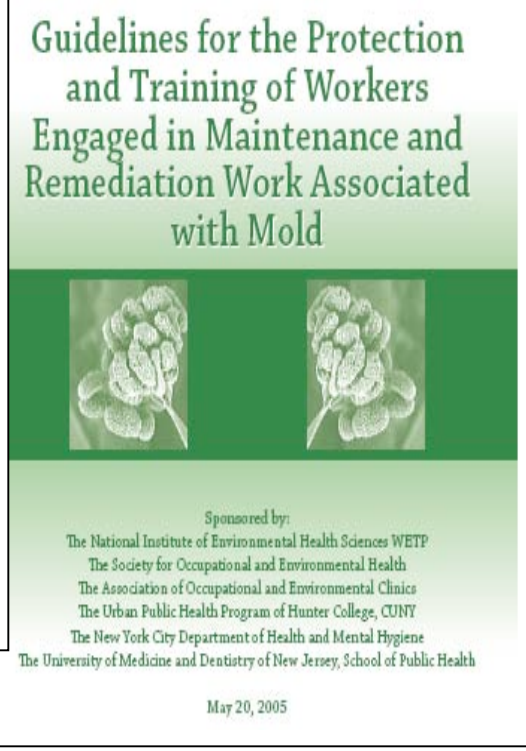
BY DELTA RICKS

Cooperative Research with CDC and EPA

CDC

Mold
Prevention Strategies and Possible Health Effects following Hurricanes Katrina and Rita
Draft, October 2005

National Center for Environmental Health
National Center for Infectious Diseases
National Institute for Occupational Safety and Health
Centers for Disease Control and Prevention



news VOA com

Voice of America September 29, 2005

Residents returning to New Orleans Find Massive Mold Growth

By Robert Raffaele

Washington, DC

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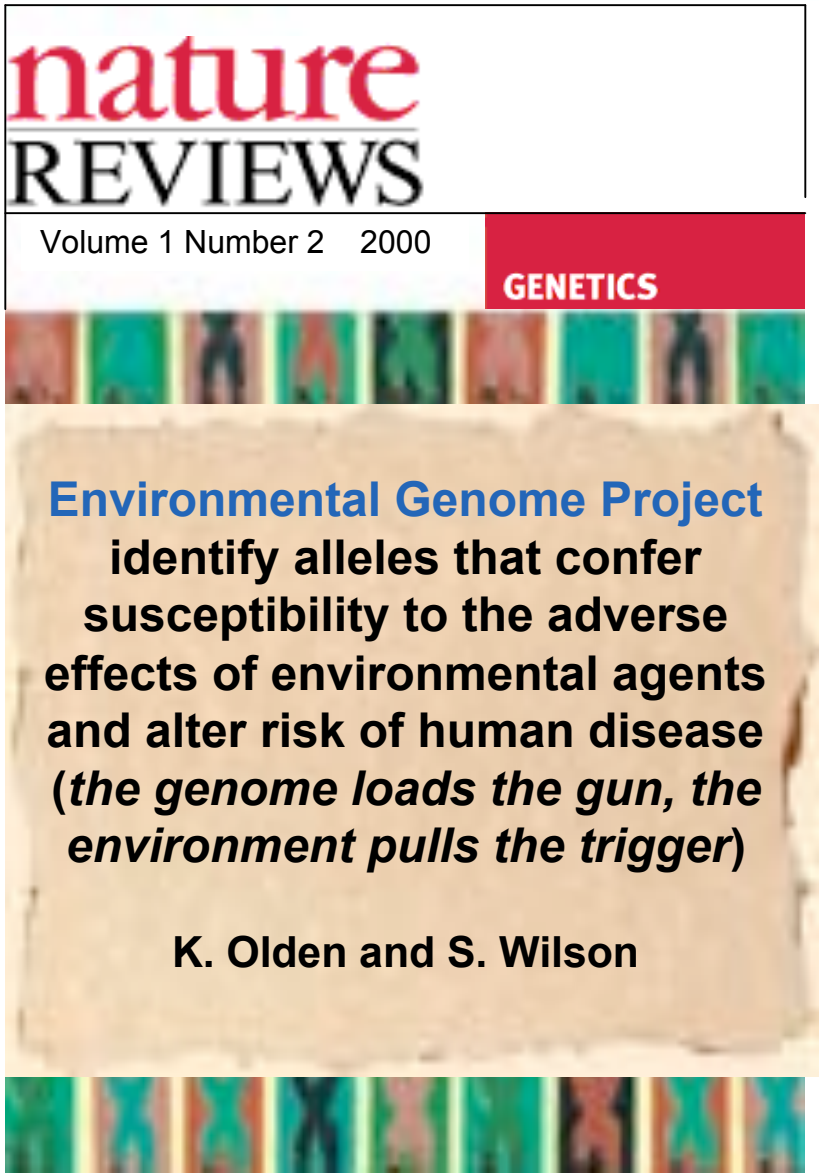

Infrastructure Needs: Environmental Genomics

- Re-sequenced > 500 "environmentally responsive" genes: cell cycle control, DNA repair, signaling, and metabolism from 90 individuals (www.genomie.utah.edu)
- Created > 50 humanized mouse strains
- Progress towards establishing standards for gene expression studies

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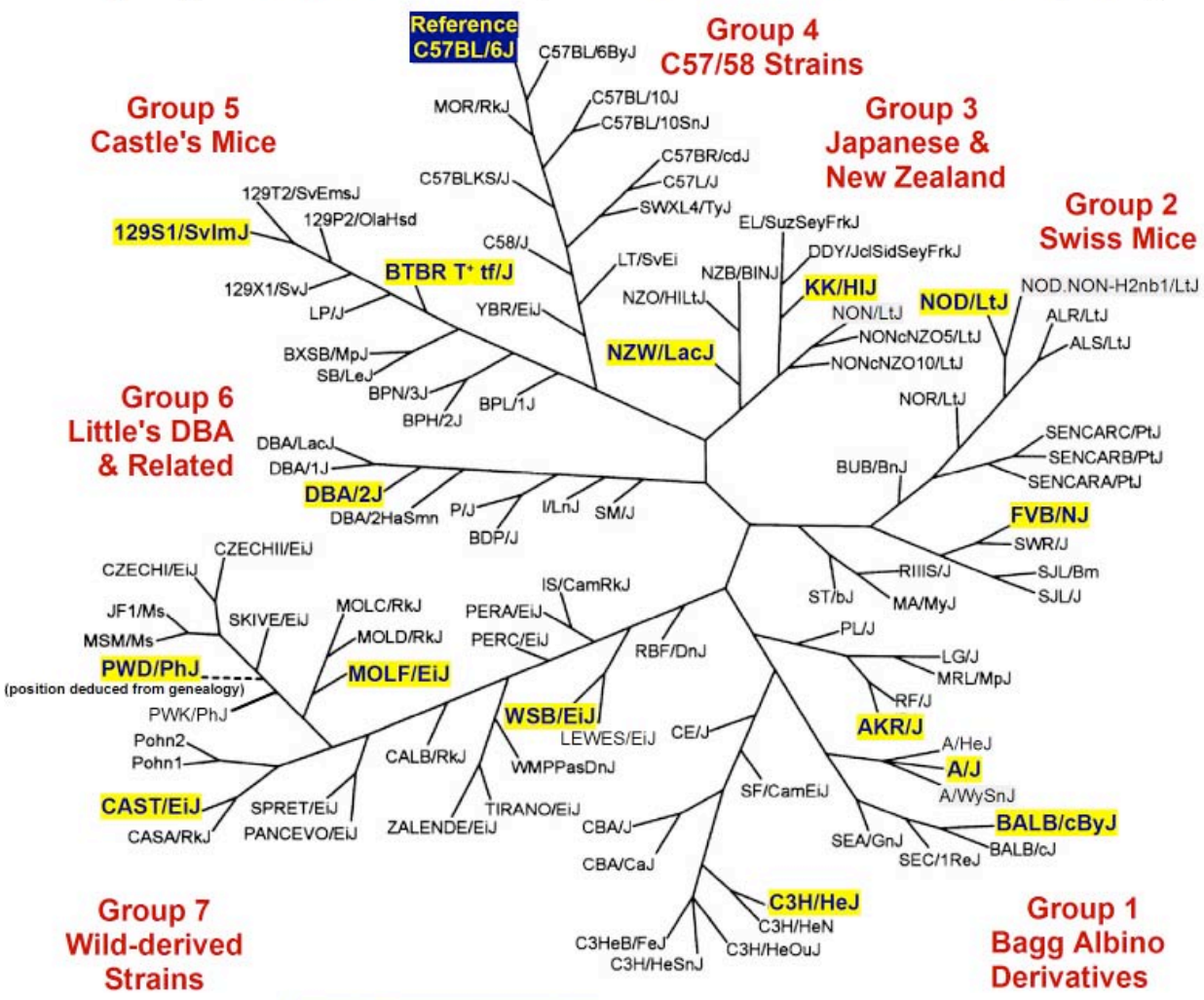
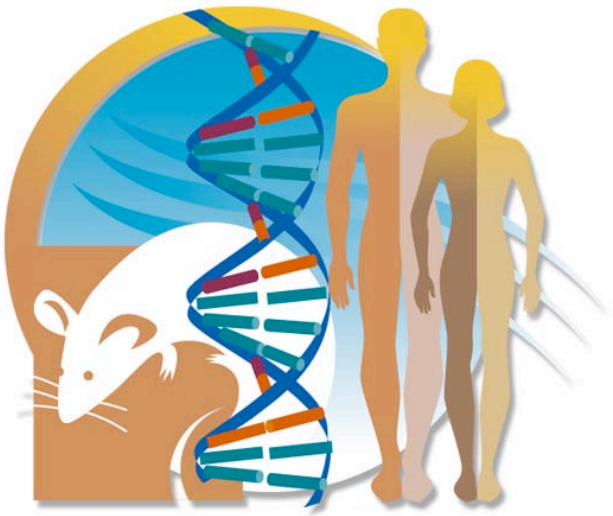
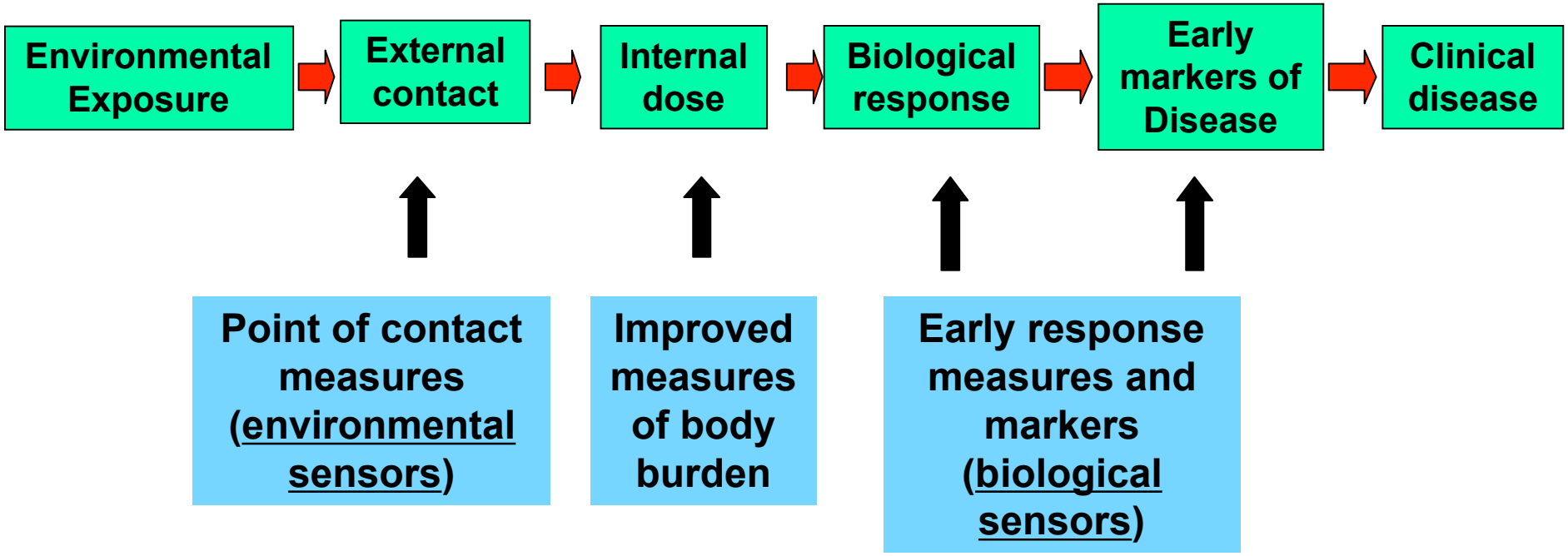
Infrastructure Needs: Comparative Genomics



Perlegen



Infrastructure Needs: More Precise Markers of Exposure



Links personal exposures to body burden to biological response

AGES – NCS Initiative

Workforce Considerations

Advancing the Nation's Health Needs: NIH Research Training Programs

Committee for Monitoring the Nation's Changing Needs for Biomedical, Behavioral, and Clinical Personnel, Board on Higher Education and Workforce, National Academy of Science, National Research Council

2005

- **A growing need exists to shorten the interval between research advances in biomedical science and the ability to apply these advances to improve the health of the public**
- **The application of lessons learned from basic science to health-related problems requires training in translational areas**

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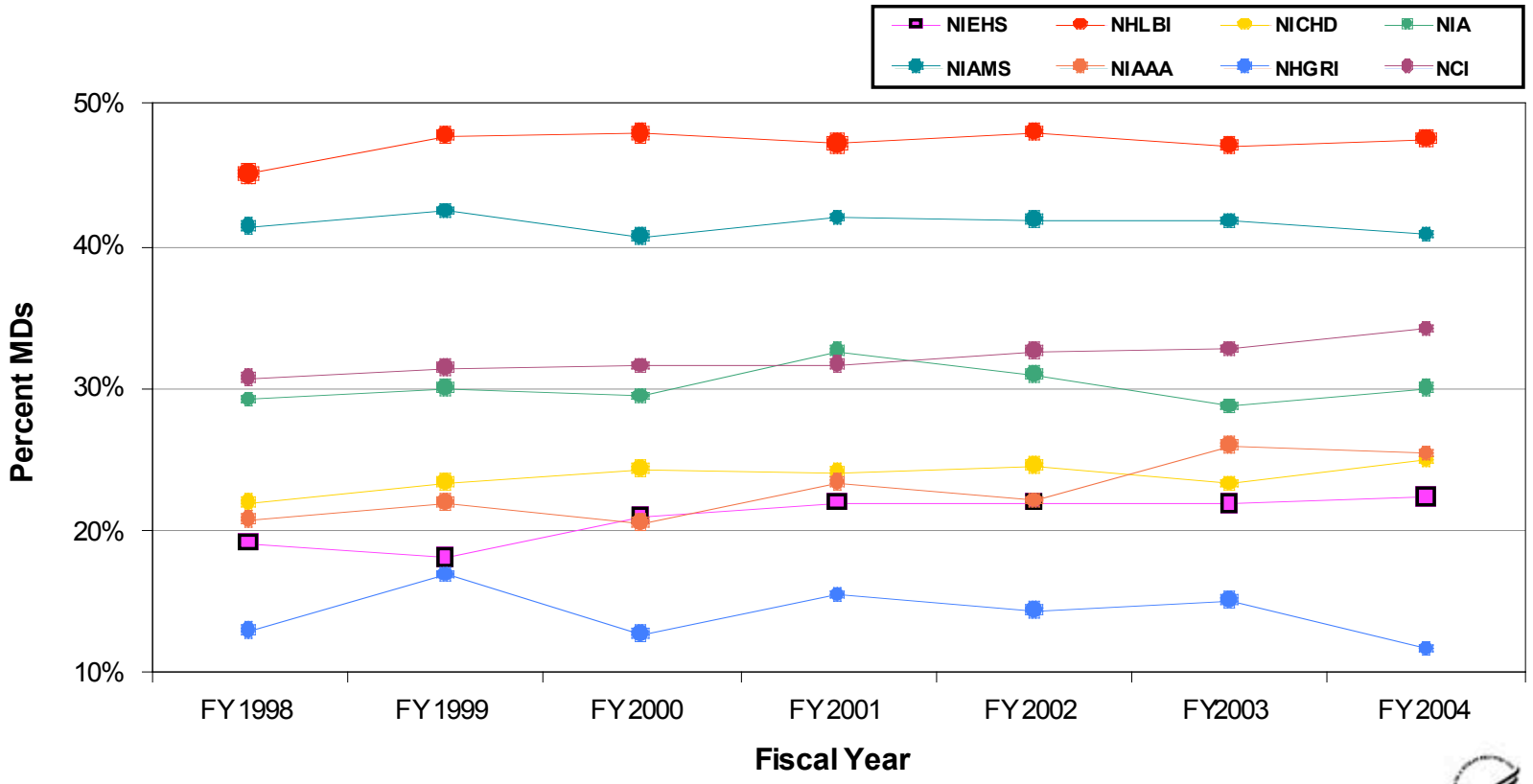
Workforce: Support scientists who will have the greatest impact on human health



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Workforce: Future Directions

- Start early and support trainees through "transition periods"
- Support training with interdisciplinary teams (basic science, computational biology, medicine, and public health)
- Focus on expanding the role of physician scientists
- Consider developing short courses in environmental sciences at NIEHS (Cold Spring Harbor or the Jackson Laboratory)

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Strategic Planning Forum: Purpose

- Establish our priorities
- Develop a plan to support the very best science that will have the greatest impact on public health
- Prepare for the future – research opportunities, recruitment, and training

Goals and objectives to guide our growth over the next 5 years

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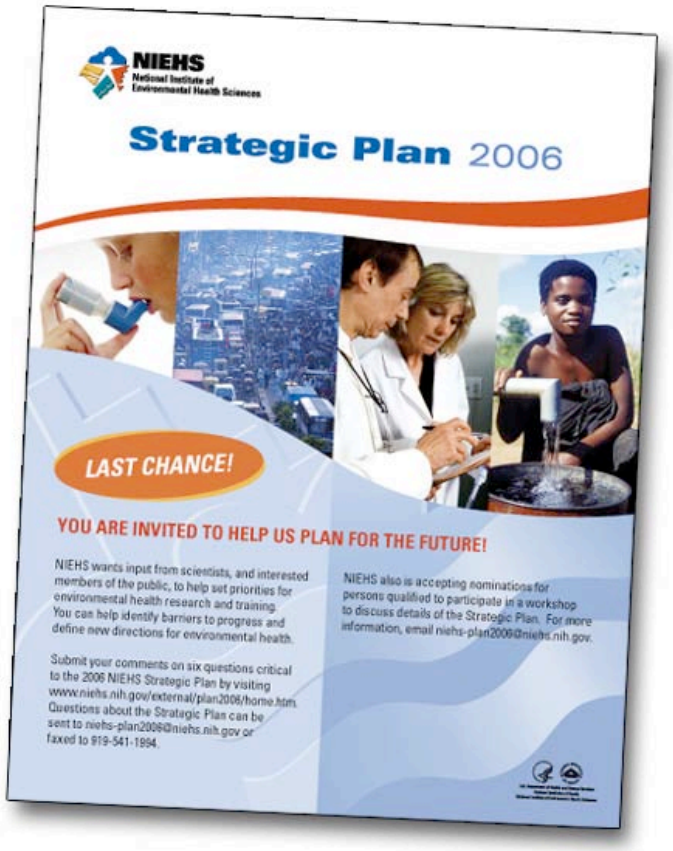
Strategic Plan: Inclusive and transparent

- Federal register and NIEHS website www.niehs.nih.gov/external/plan2006/home.htm
- Steering Committee
- Strategic Planning Forum
- Draft document available for public comment
- Final document released in early 2006



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Strategic Planning Forum

Multiple perspectives: academia, government, industry

Varied expertise: biomedicine, genetics, toxicology, clinical medicine, epidemiology, engineering, statistics

Research Discussion Areas:

- **Human biology**
- **Human health and disease**
- **Infrastructure investment**
- **Exposure sciences**
- **Global environmental health**
- **Training**

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Guiding Principles for Program Development

- Best science – highest impact
- Focus on human health and disease
- Support investigator initiated research
- Support the young investigator
- Partnerships
- Entrepreneurial/Opportunistic
- Listen to our stakeholders

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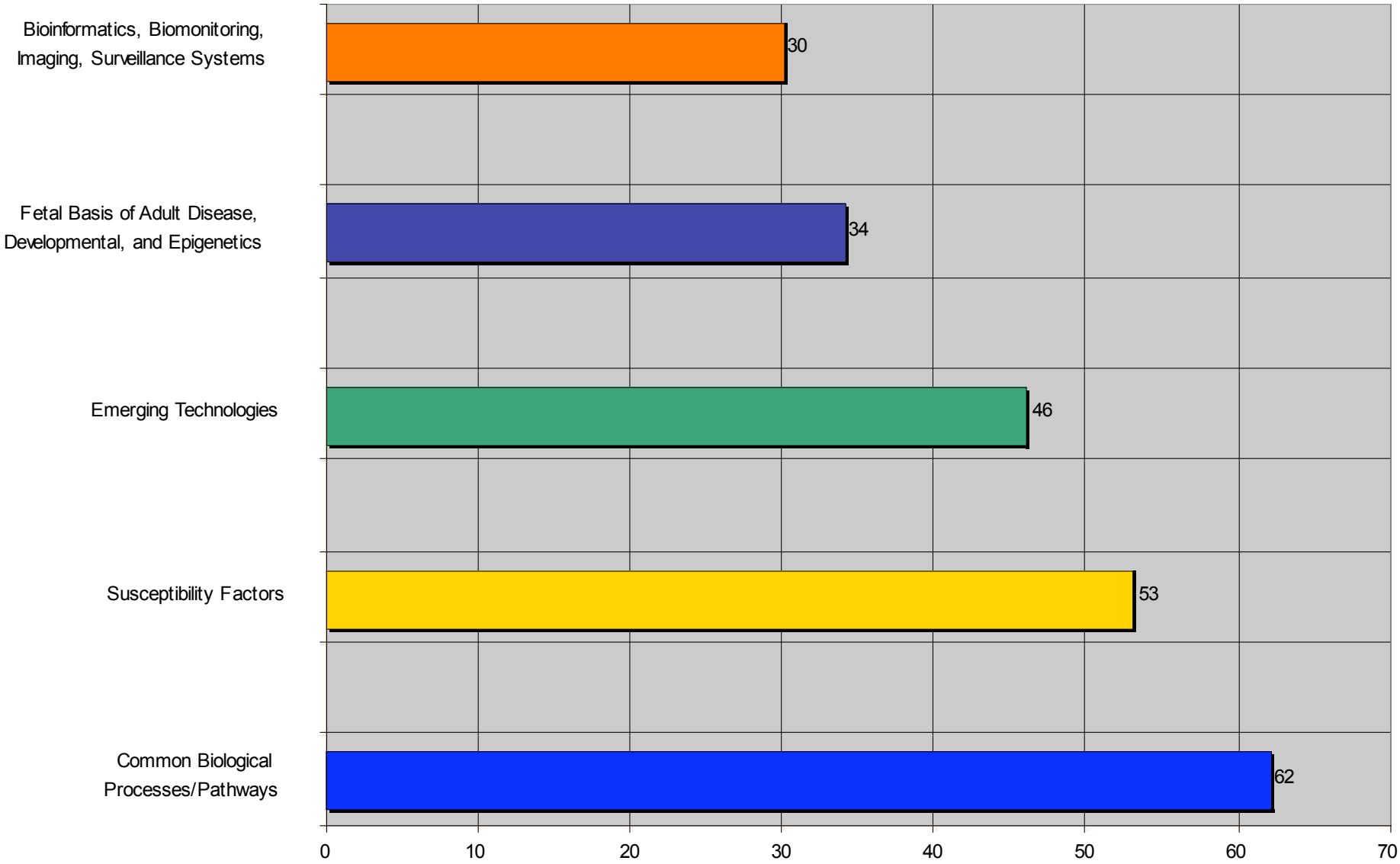
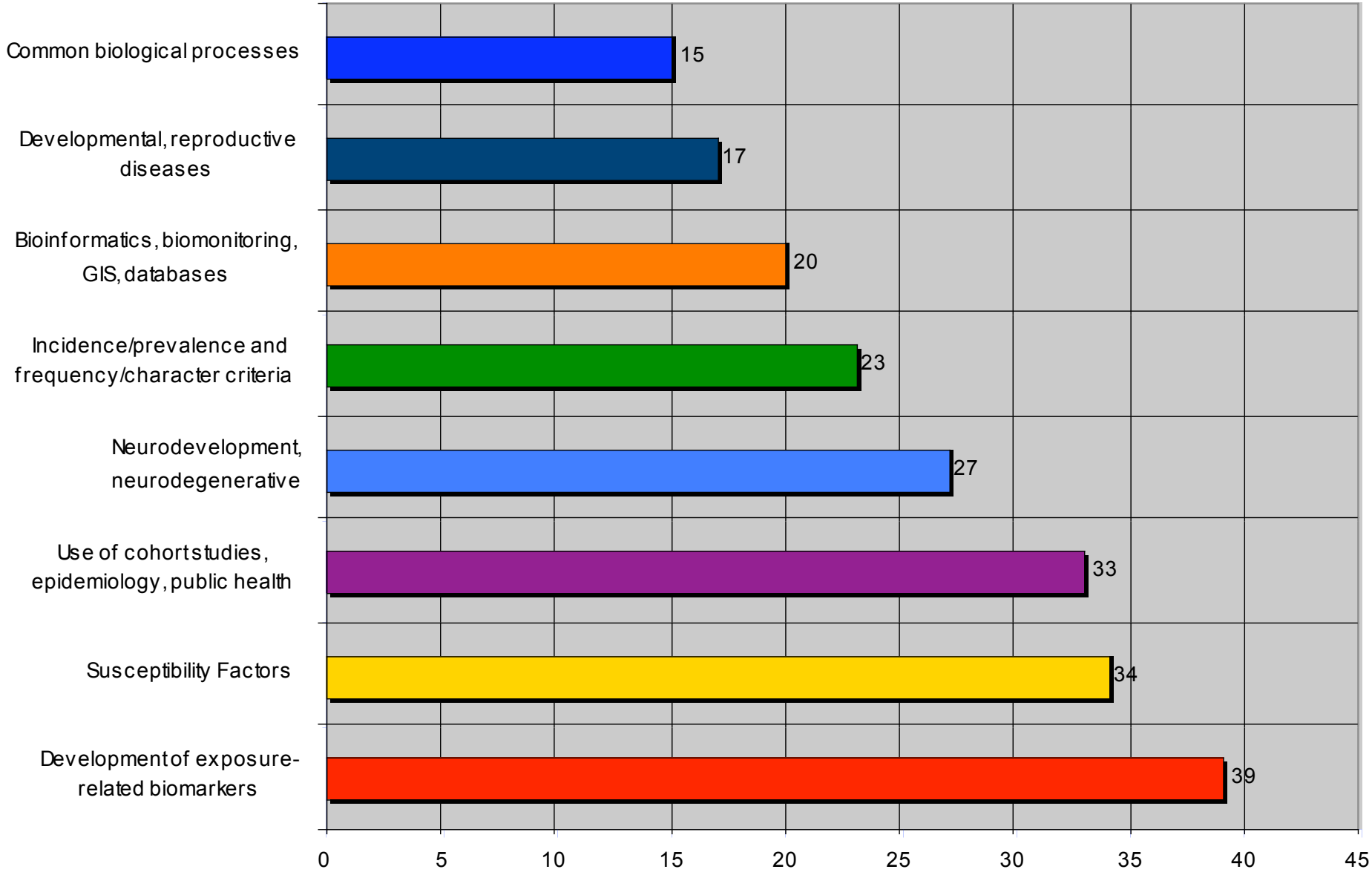
Prioritizing and Program Development

- Human Health and Disease
  - Specialized Centers in Environmental Health
  - EHSRCs
  - ONES Program
  - Enhance role of physician scientist
- Exposure Biology Initiative (NHGRI and NICHD)
- Environmental Genomics
  - Epigenetics
  - Comparative biology/genomics
  - Training in environmental genomics
- Global Environmental Health

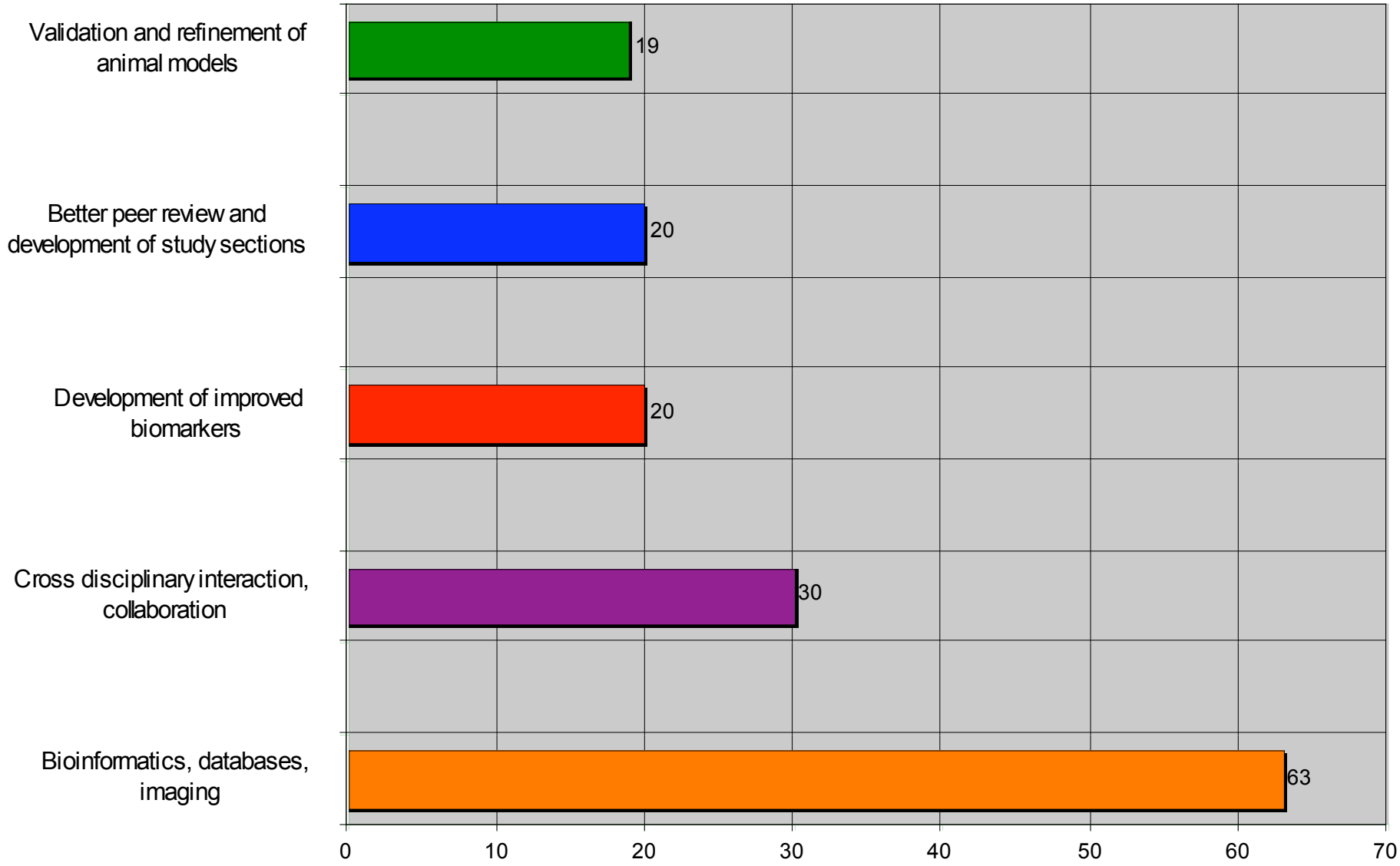
Using Environmental Sciences and Environmental Exposures to Understand Human Biology



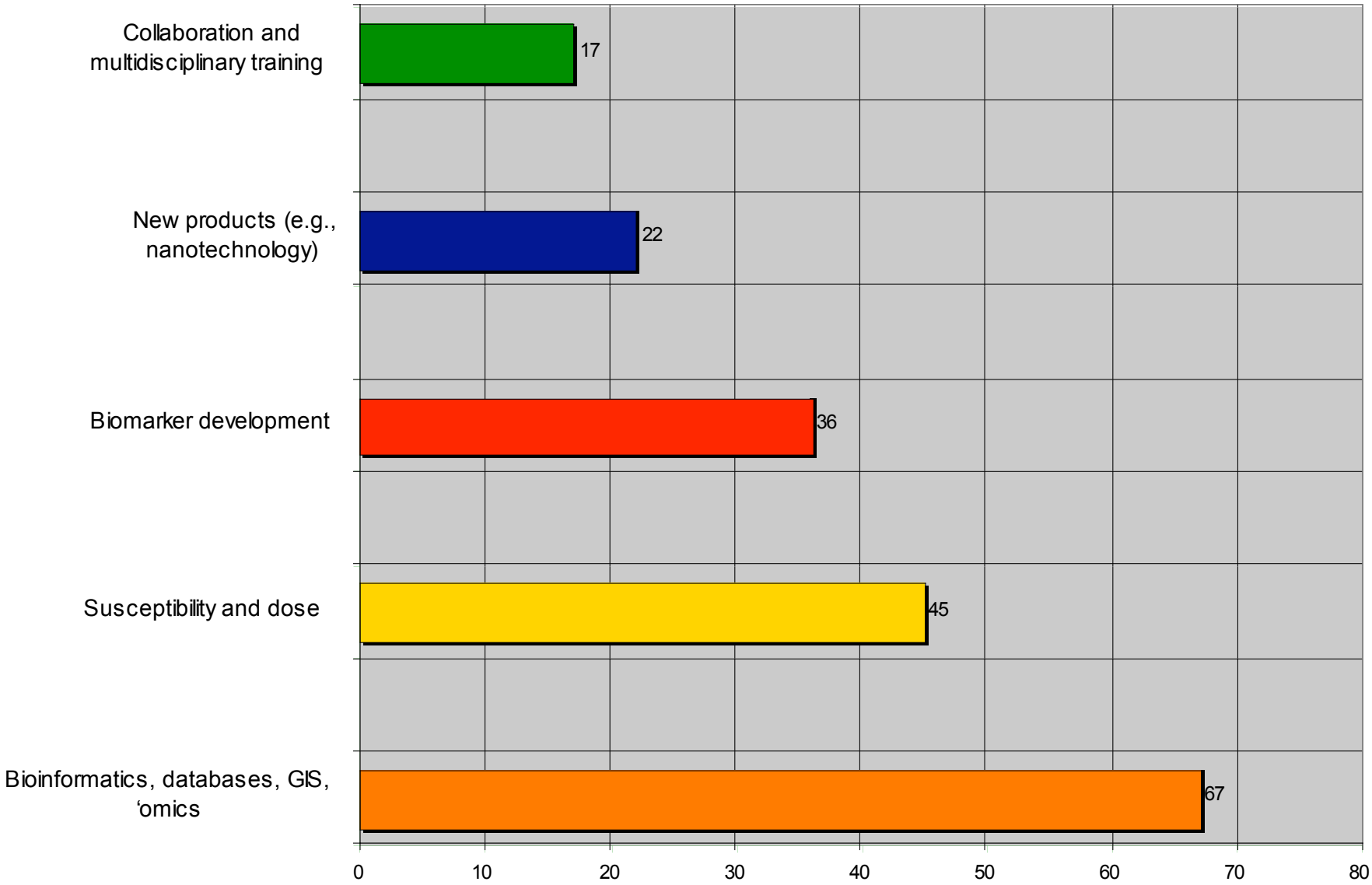
Using Environmental Sciences and Environmental Exposures to Understand Human Diseases and Improve Human Health



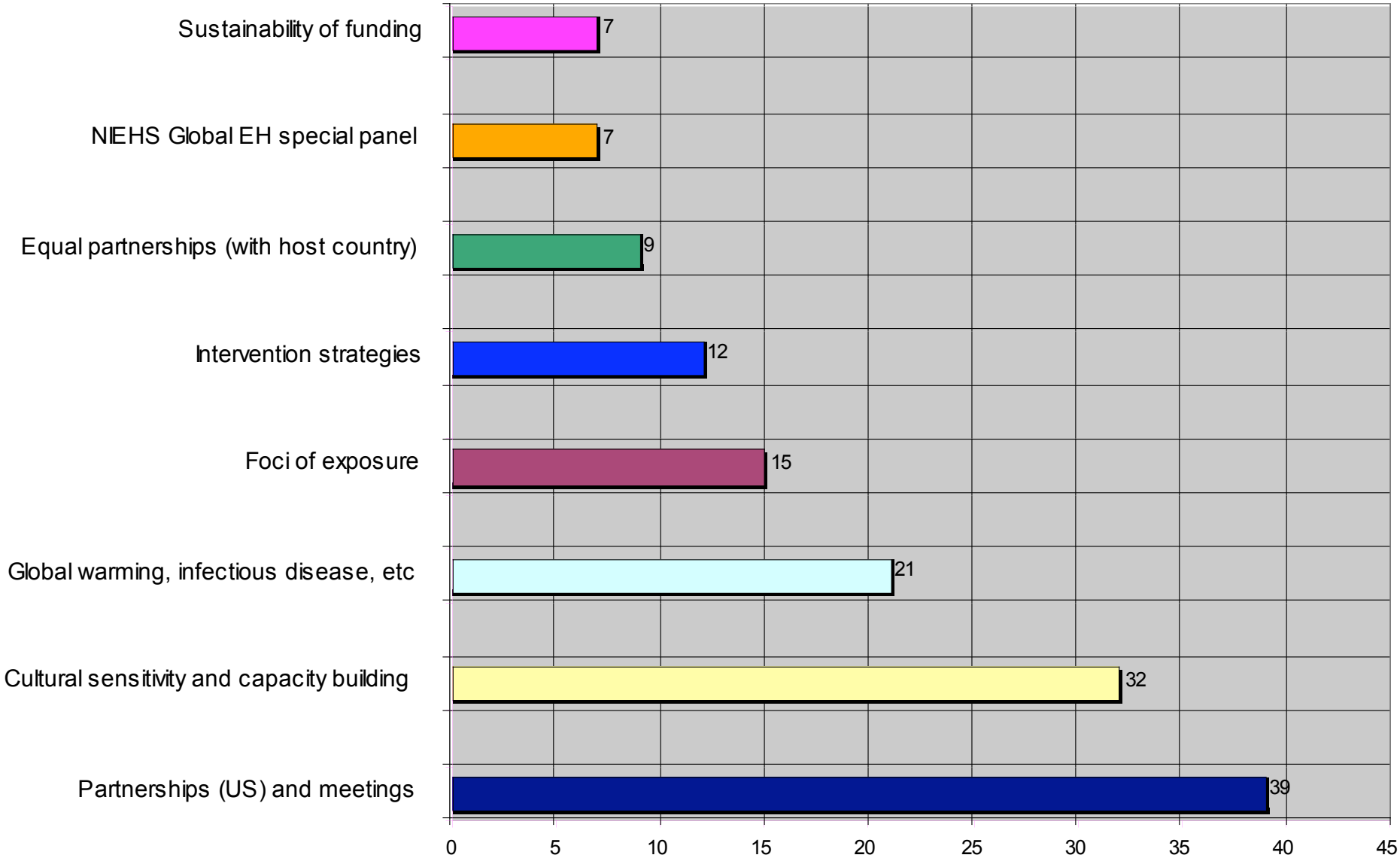
Infrastructure Investment: Technological Needs and Applications

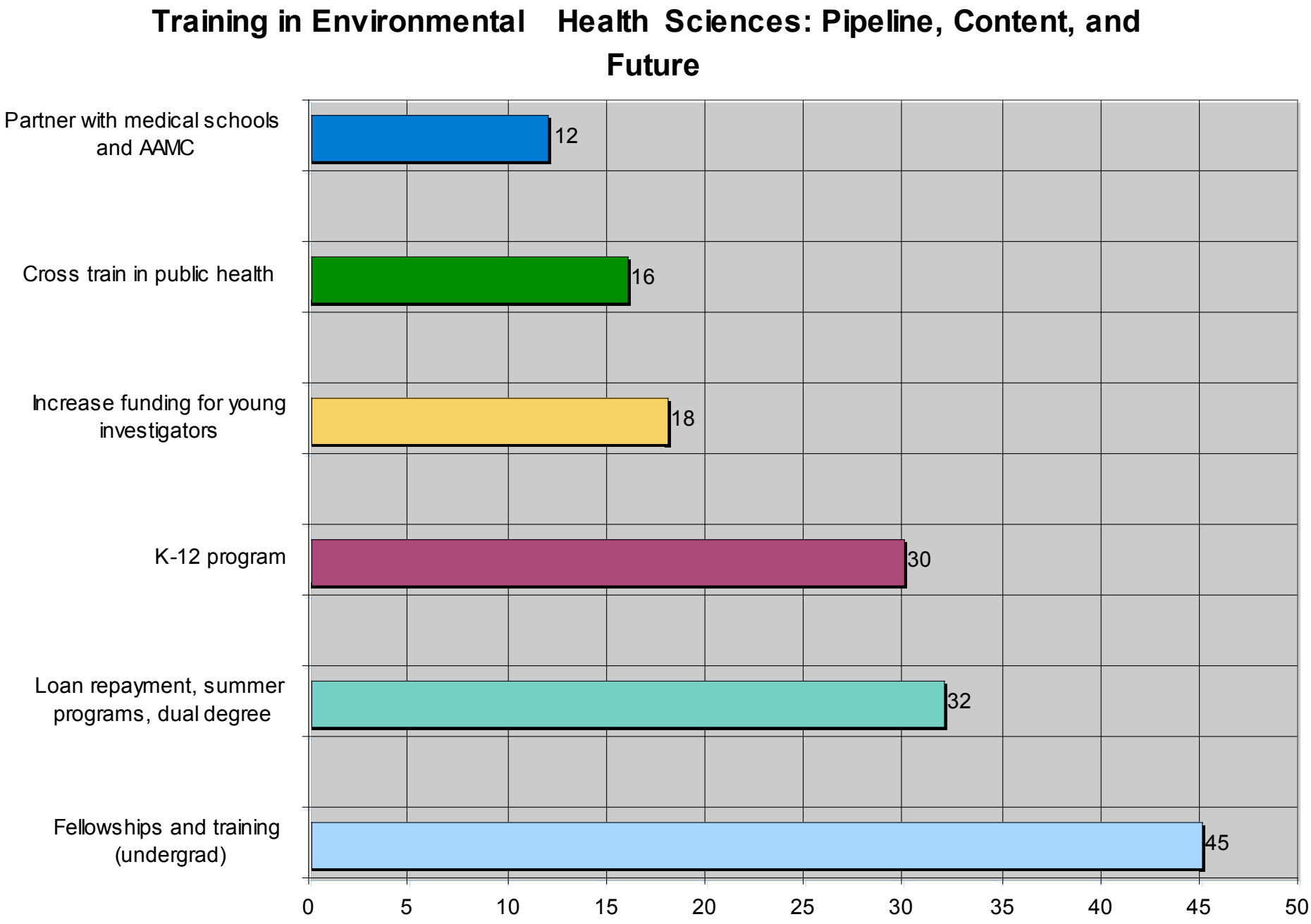


Exposure Sciences: Needs, Opportunities, and Challenges



Global Health: Environmental Health Priorities and Opportunities




Training in Environmental Health Sciences: Pipeline, Content, and Future
Partner with medical schools and AAMC
12
Cross train in public health
16
Increase funding for young investigators
18
K-12 program
30
Loan repayment, summer programs, dual degree
32
Fellowships and training (undergrad)
45
0
5
10
15
20
25
30
35
40
45
50

NIH Reauthorization

- Division of Program Coordination, Planning, and Strategic Initiatives – extension of the NIH Roadmap
  - emerging scientific opportunities
  - rising public health challenges
  - involvement of multiple ICs
- Common Fund – start at 1% but will grow to 5% (2006 - 330 million; 2008 – 520 million)
- ICs maintain their individual appropriation

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Helping People Live Longer Healthier Lives

Training

Global Environmental Health

Basic Science

Disease-Focused Research

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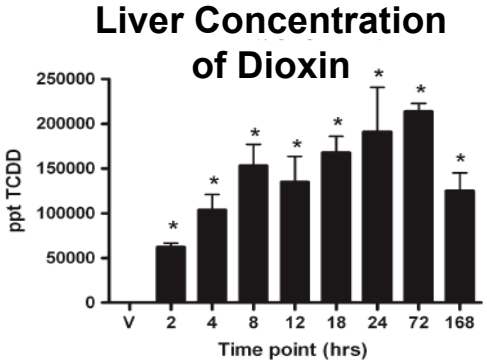
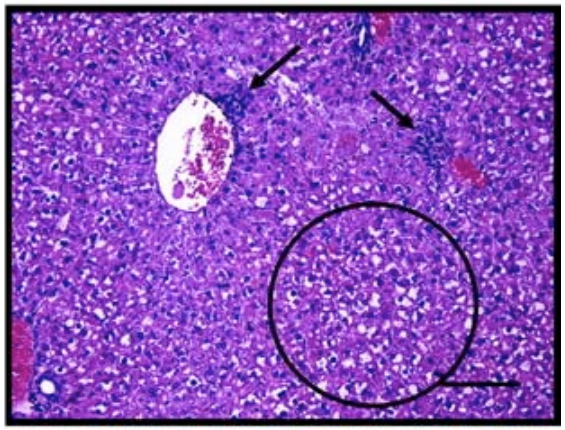
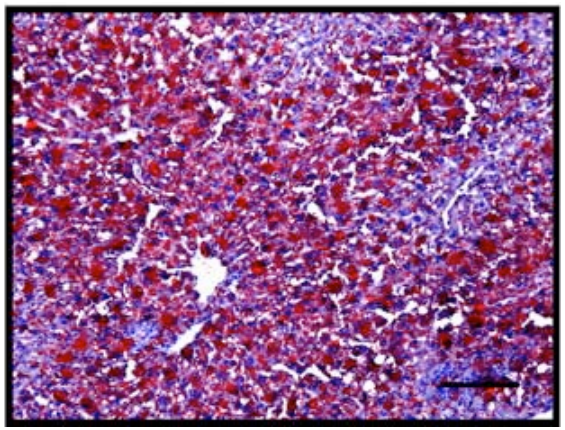
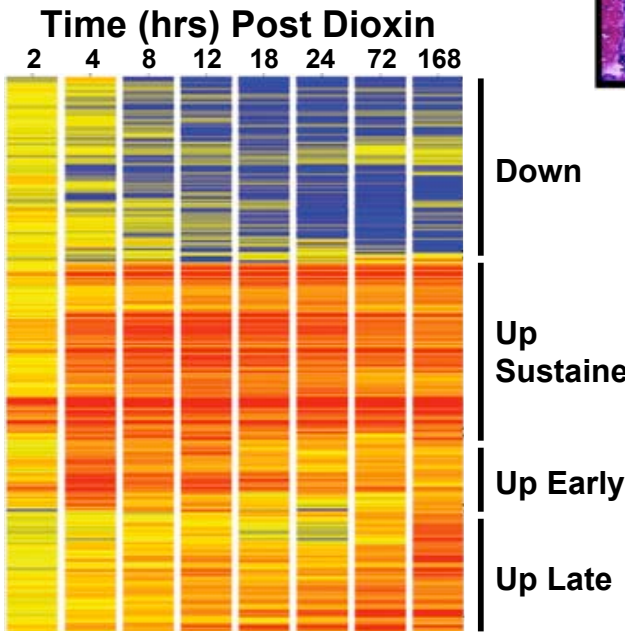
Transcriptional Response to Dioxin Reveals Underlying Mechanism/Pattern









- Gene expression preceded histopath changes
- Metabolism (Cyp1a1), oxidative stress (Nqo1), FA metabolism, and gluconeogenesis
- Novel genes and mechanisms identified
- Pattern of response unique to dioxin (also shown for genotoxic vs. nongenotoxic carcinogens)

Boverhof. *Tox Sciences* 2005; 85:1048

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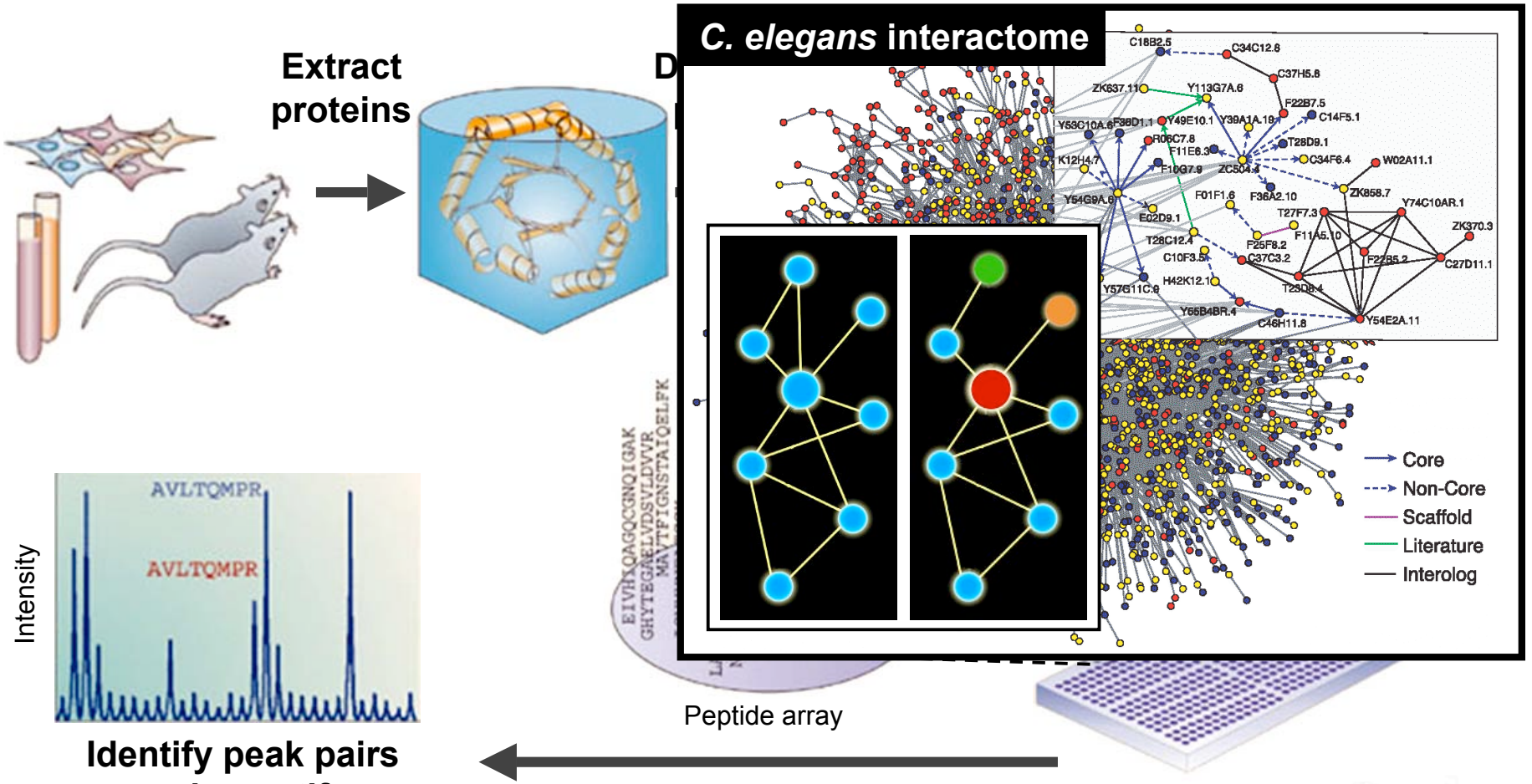
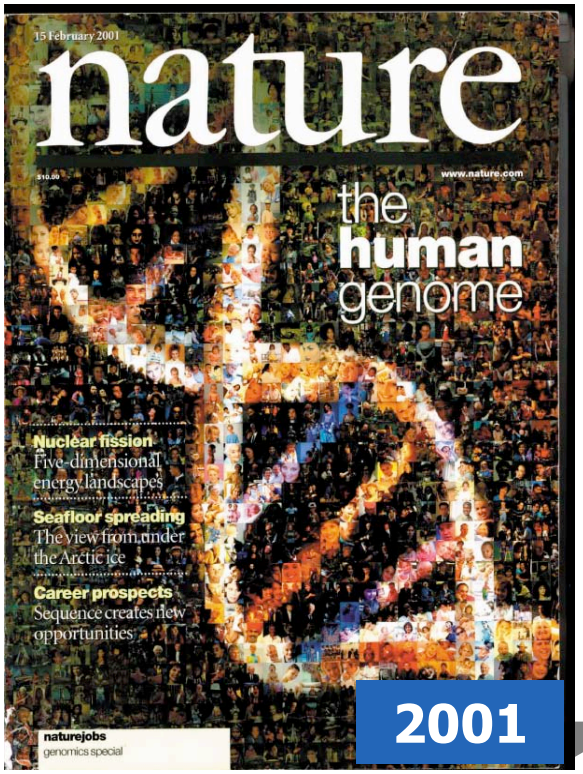
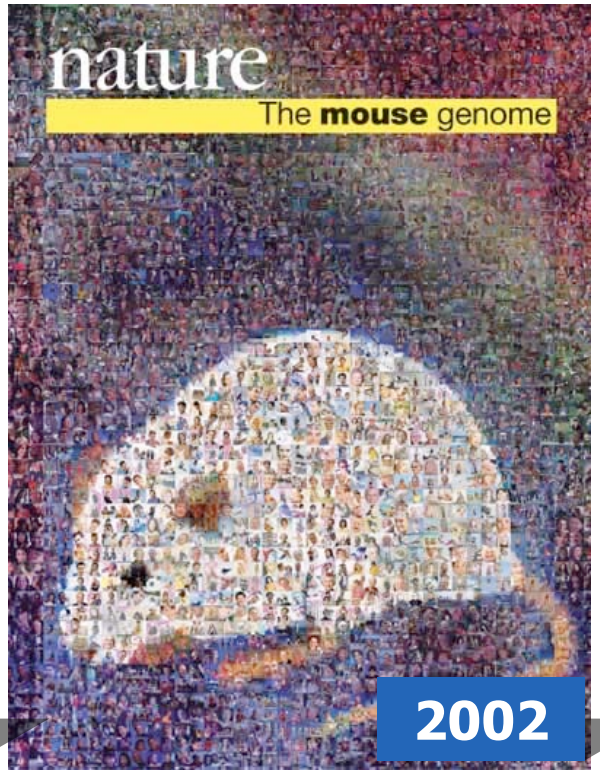
Scoring Proteomes: Essential for Biosensors



Kuster. *Nat Rev Mol Cell Bio* 2005; 6:577

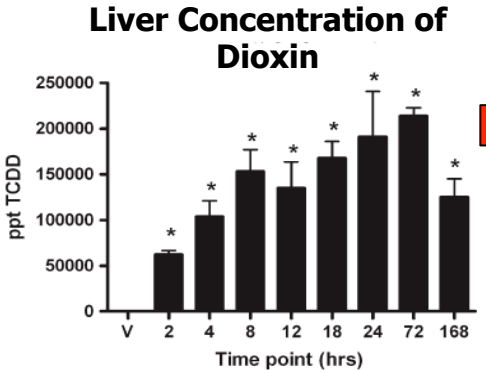


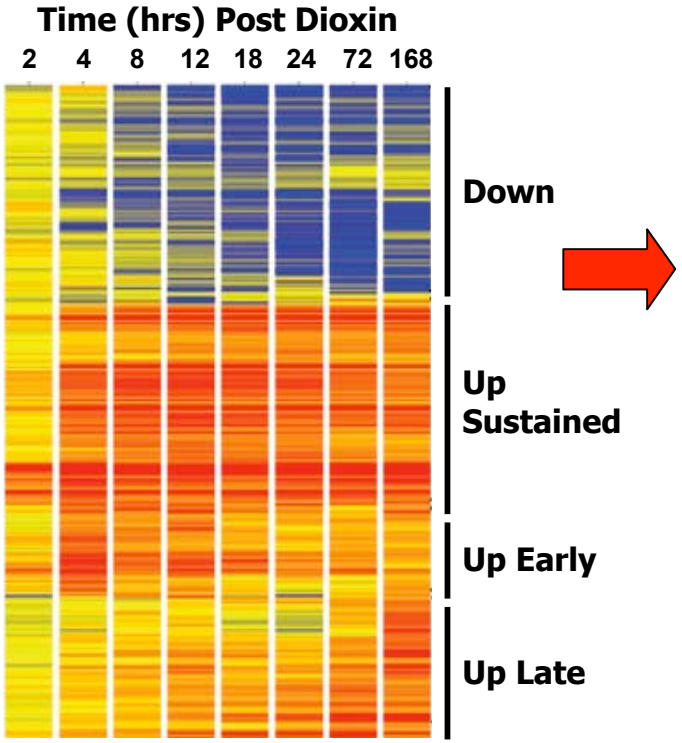


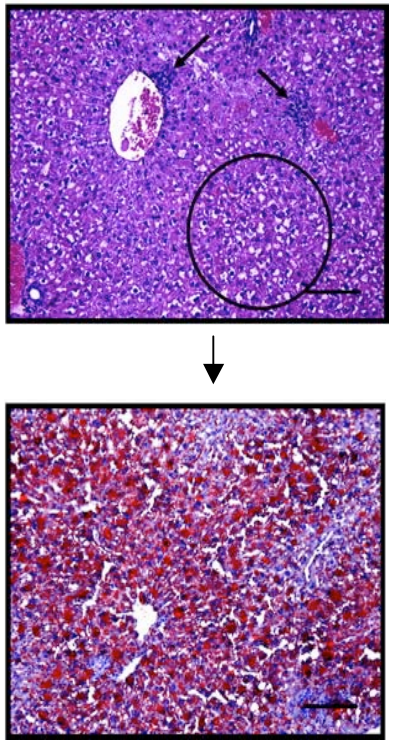
Genes are only a small part of our make-up; the environment has a spectacular impact

Eric Lander

Transcriptional Approach to Reveal Dioxin Mechanism







Toxicology:

Time course of target organ dose

Gene Expression:

- Precedes histopathology
- Novel genes/mechanisms: metabolism (Cyp1a1), oxidative stress (Nqo1), FA metabolism, and gluconeogenesis
- Pattern unique to dioxin, and genotoxic vs. nongenotoxic carcinogens

Histopathology:

Changes correlate with target organ dose and gene expression

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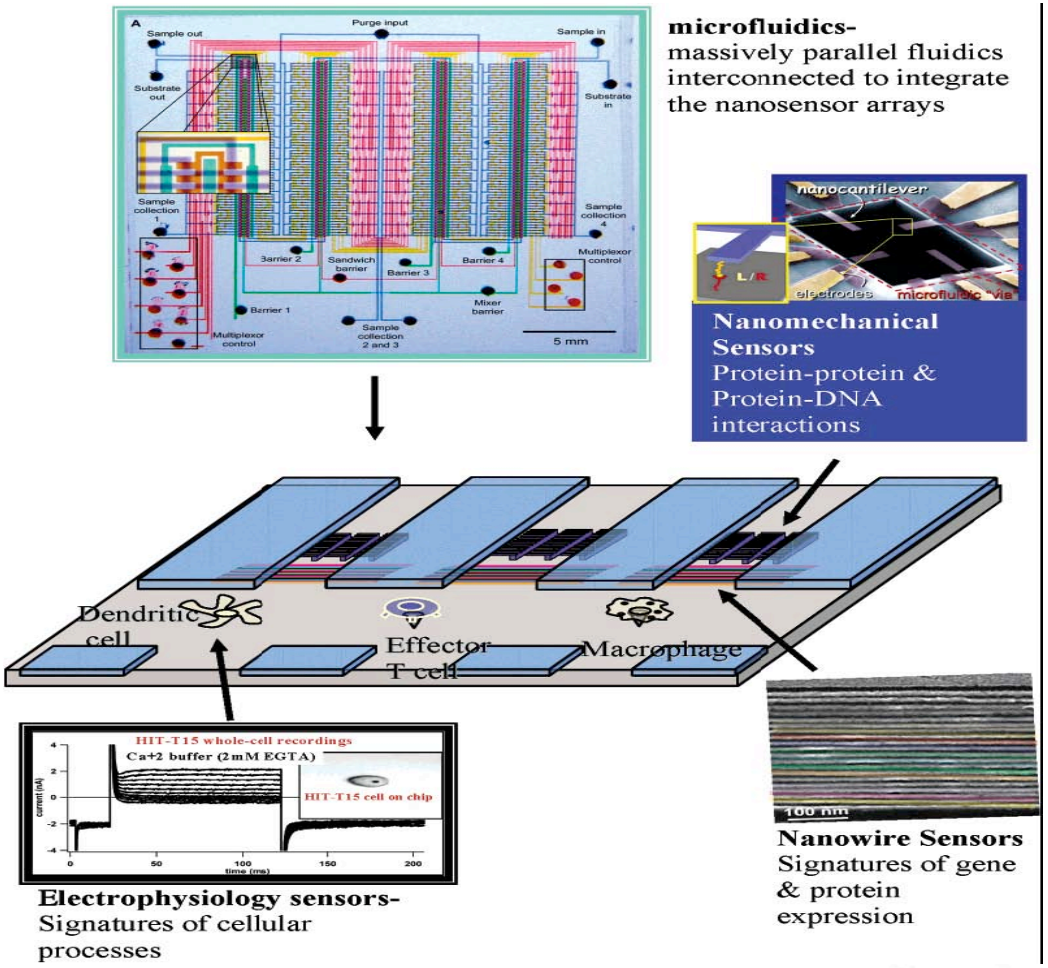
Mutiparameter Analysis of Exposure

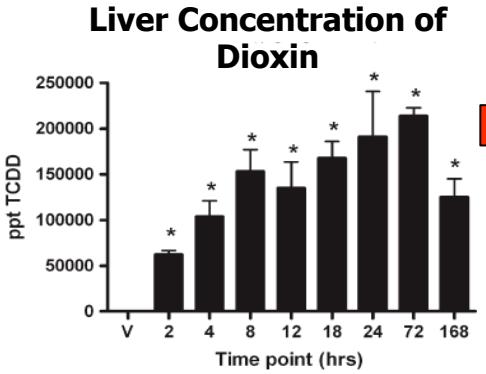
Micro- and Nanoscale sensing devices that combine existing assays:

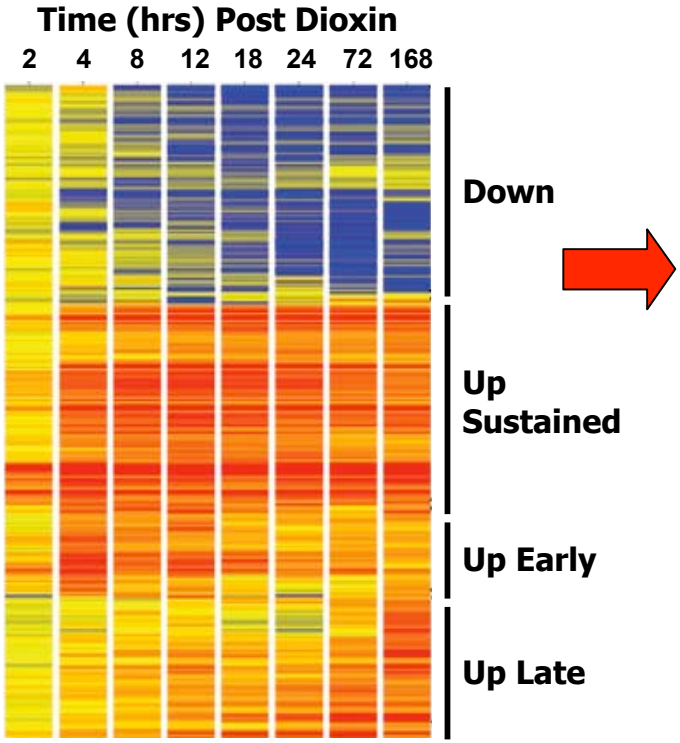
- DNA sequencing
- DNA gene expression
- Proteomics
- Metabolomics

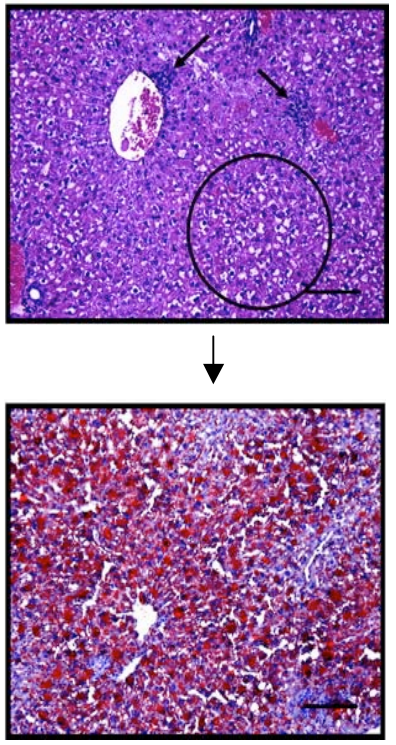


Watson and Hood, J Prot Res. 2004

Transcriptional Approach to Reveal Dioxin Mechanism







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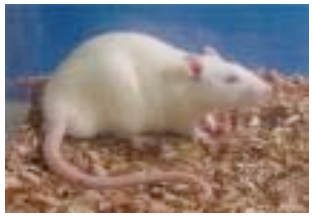
Transgenerational Effects of Endocrine Disruptors



X

F_0 Parents

Male S-D rat

Female S-D rat

No exposure

Daily exposure to vinclozolin or methoxychlor

F_1 male x F_1 females from different litters

X 4

Outcross: Vinclozolin-treated F2 males X WT untreated females

Reverse outcross: vinclozolin-treated females X WT untreated males

Transgenerational effects seen in >90% all males, all generations:

- ↑ spermatogenic cell apoptosis
- ↓ epididymal sperm count and motility
- ■ Loss of germ cells and abnormal seminiferous tubules (F_3 males)

No effect on spermatogenic cells: transgenerational phenotype transmitted through male

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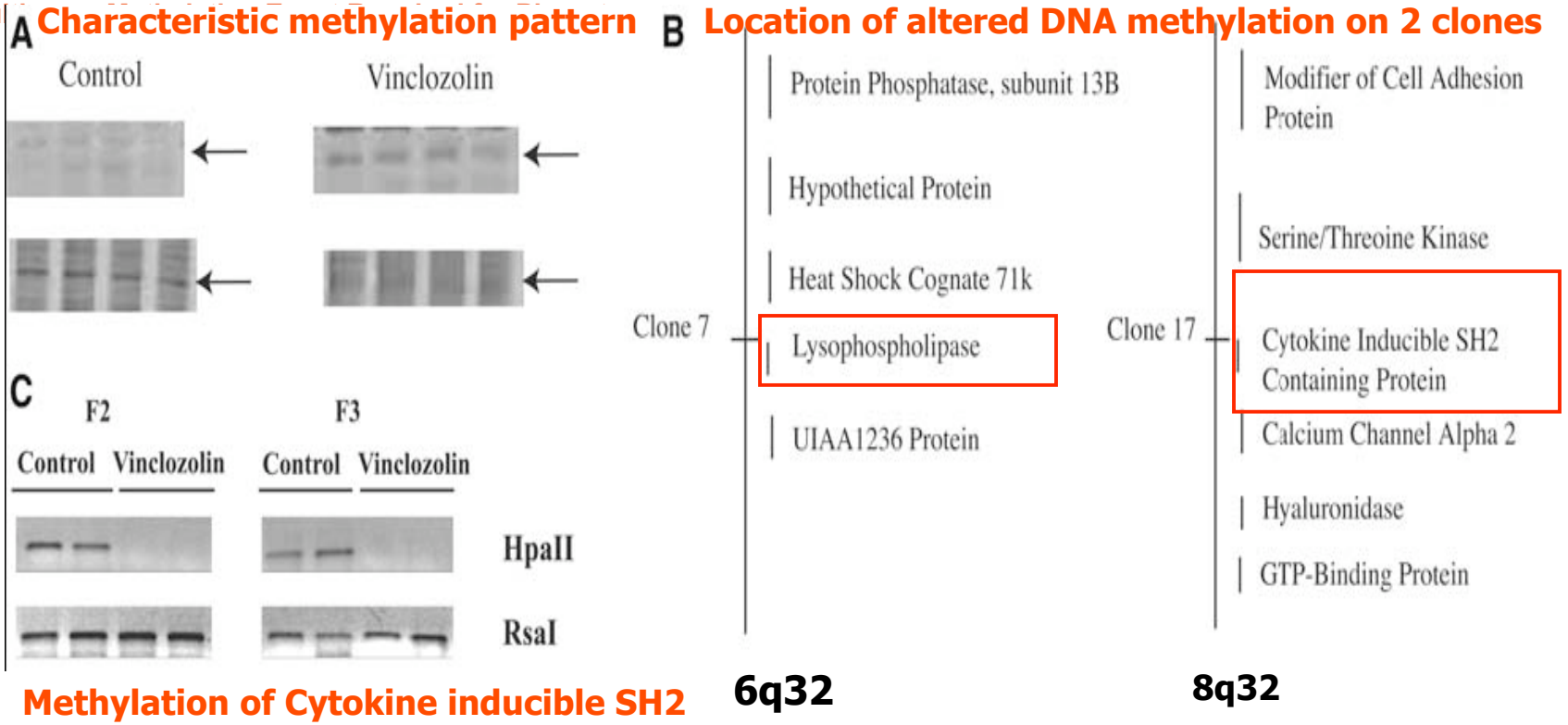
Mu



Methylation of Cytokine inducible SH2

DNA methylation pattern from vinclozolin-treated and control animals:

- 25 PCR products with altered DNA methylation from treatment
- Characteristic pattern of DNA methylation seen in treated vs. control animal
- Two DNA fragments mapped to chromosome 6q32 (clone 7) and chromosome 8q32 (clone 17): lysophosphotase and cytokine inducible SH2 protein possible epigenetic markers

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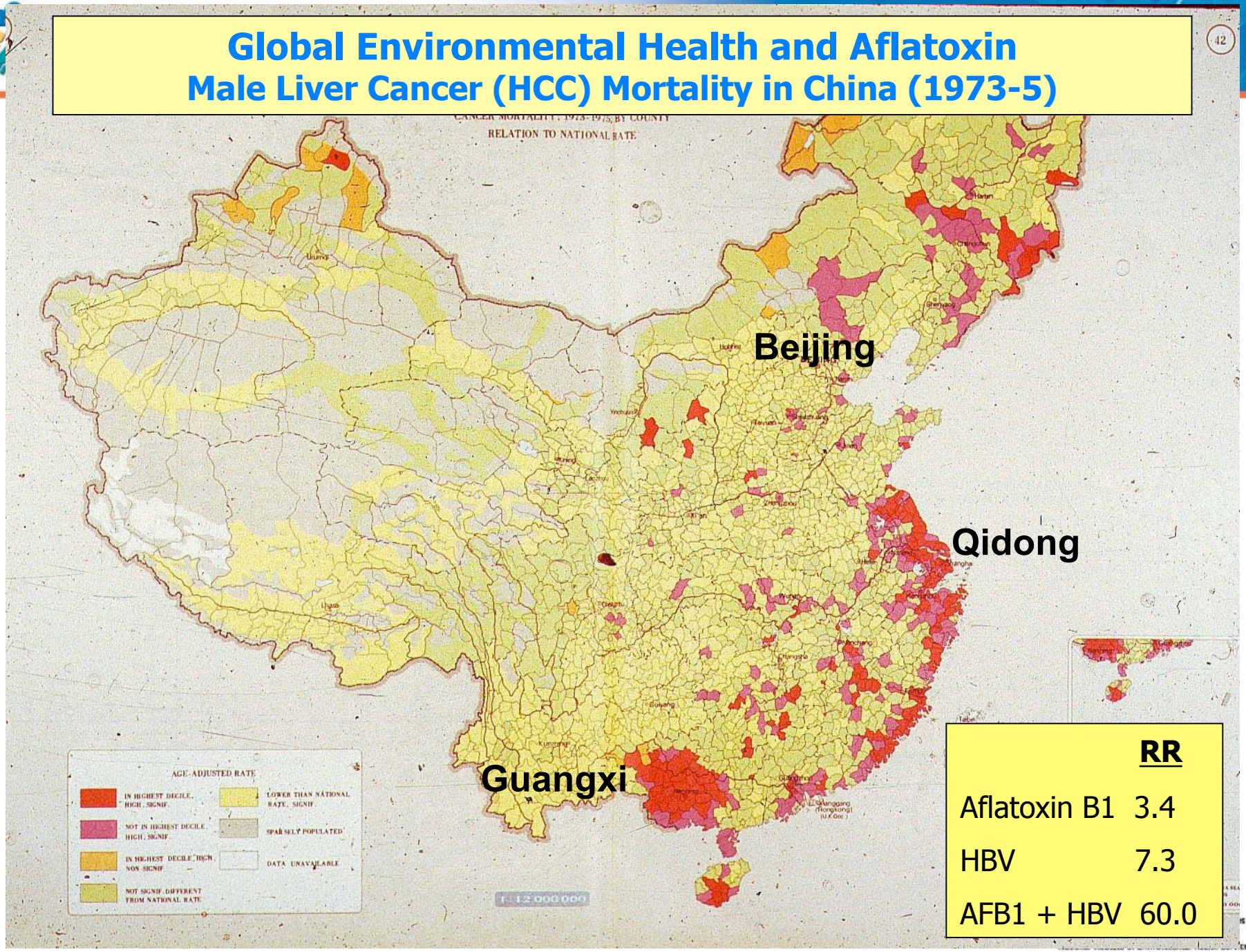
Global Environmental Health

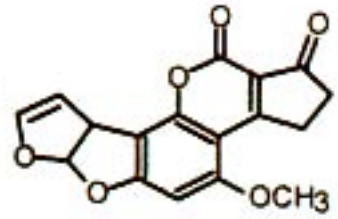
- Impact of environmental toxicants can be far-reaching; crossing all borders
- Over 5 million children each year die from illnesses caused by the environment
- 1/3 of all illnesses in the world are attributable to environmental factors

Global Environmental Health and Aflatoxin
Male Liver Cancer (HCC) Mortality in China (1973-5)



	RR
Aflatoxin B1	3.4
HBV	7.3
AFB1 + HBV	60.0

Aflatoxin Research (1959-2005)



1959 Aflatoxin Named

1961 Liver Cancer in Rats

1963 ★ Structures Elucidated

1967 ★ Toxicology and Metabolism

1968 ★ Levels in Thai Diet vs Liver Cancer

1972 First IARC Evaluation

1977 ★ DNA Adduct Identified

1981 ★ DNA Adduct in Urine

1984 ★ Monoclonal Antibodies and IAC

1987 ★ Albumin Adduct Identified

1988-92 ★ Food Intake/ Biomarkers China & Africa

1992 ★ Aflatoxin/HBV and HCC in PRC and Africa

1992, 1999 ★ HBV Modifies Biomarkers in Children

1994 Aflatoxin is a Group 1 Human Carcinogen

1997-2005 ★ Oltipraz/ Chlorophyllin/ Broccoli Sprouts Clinical Trials

2002-2005 ★ p53 and HBV mutations in plasma

★ **Supported by NIEHS P01 and T32 Grants**

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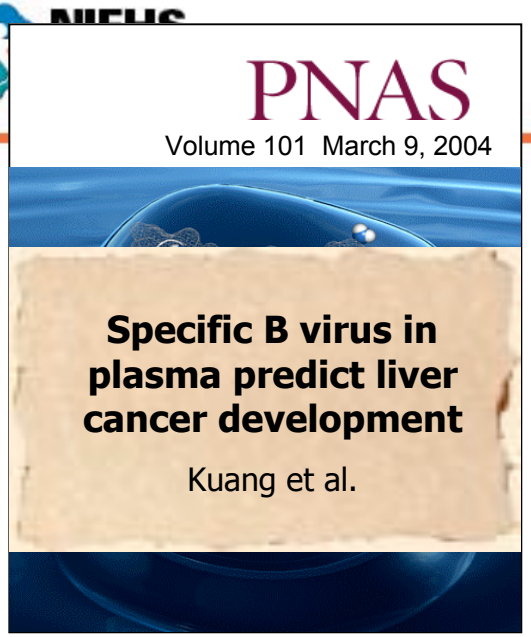

- **129 residents of Qidong, China monitored for 10 yrs for aflatoxin exposure and HBV**
- **Determined temporality of HBV mutations in plasma and tumors**
- **Identified pre-diagnosis markers of specific HBV mutations in plasma**

- **Incidence liver cancer in men associated with AFB1**
- **AFB1-N-gua in urine correlate with AFB1 dose (rat)**
- **AFB1-N-gua correlate with AFB-DNA adduct levels in liver (rat)**
- **Liver AFB1-DNA adduct correlate with tumor incidence (rat)**
- **AFB1-N-gua in urine correlate with aflatoxin intake (humans)**

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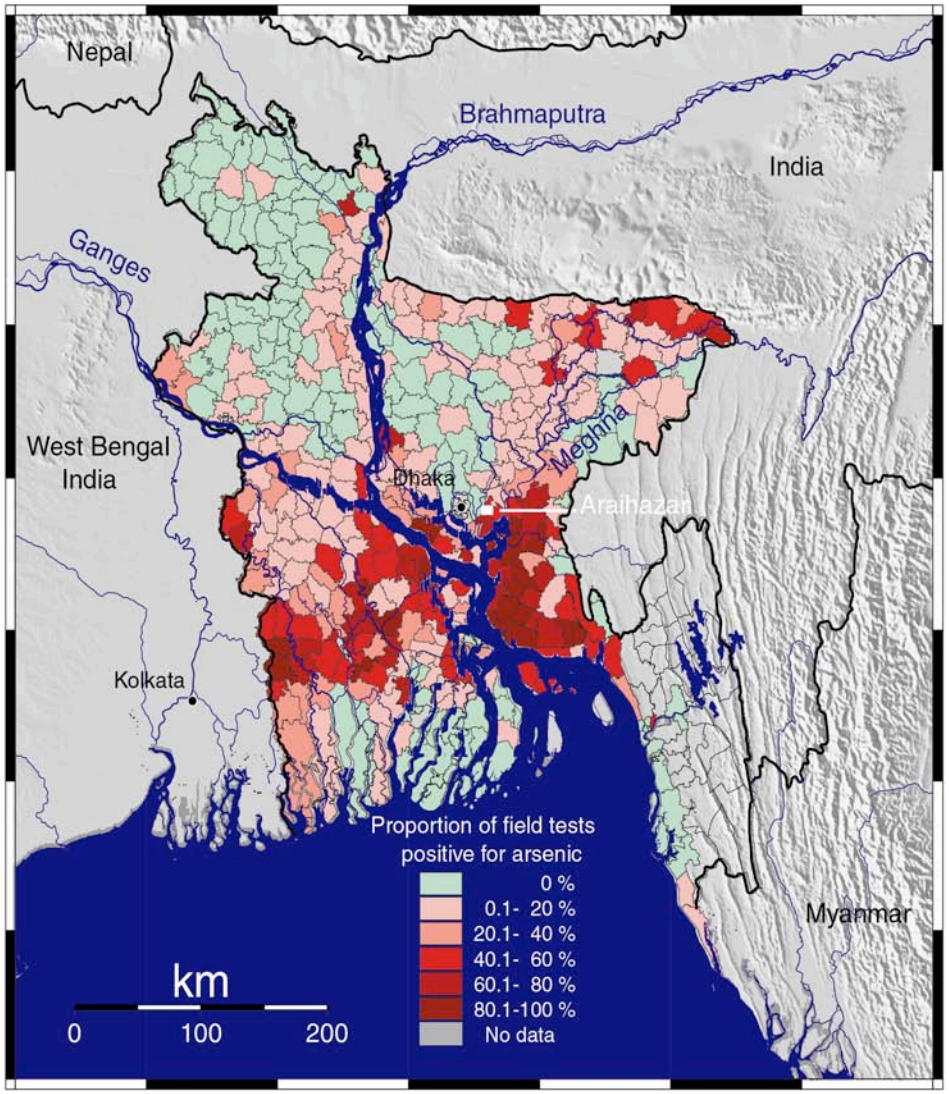

- **30-36 million people chronically exposed to high levels of arsenic in drinking water derived from ground water in Bangladesh**
- **Arsenic contamination a problem identified in mid-1990s**
- **Large regional variation in exposure levels, difficult to assess actual exposure**
- **Skin cancer a major health problem**

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World Health Organization

World Health Organization Bulletin 2002

Promotion of well-switching to mitigate the current arsenic crisis in Bangladesh

Van Green et al.

Cancers of the skin, liver, lungs, as well as diabetes and cardiovascular diseases induced by the presence of arsenic in water will contribute to a major human tragedy over the next several decades

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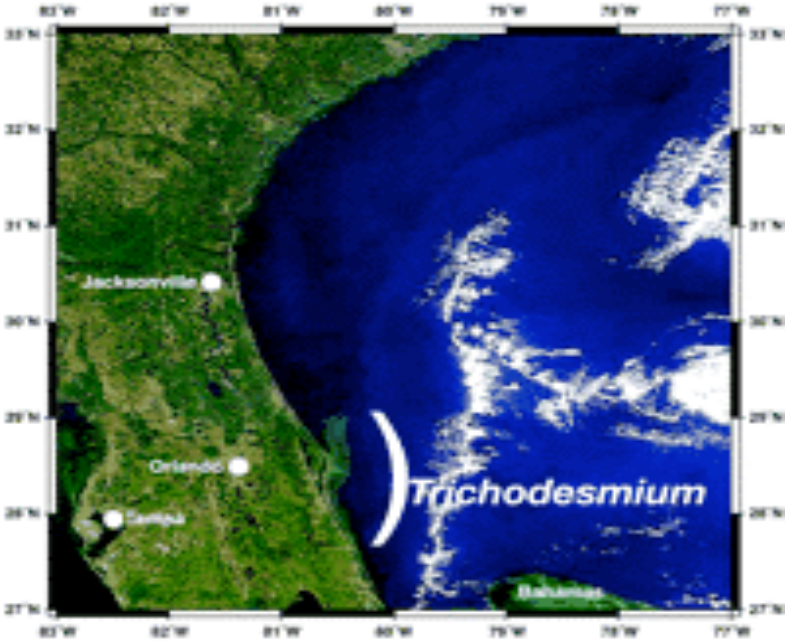

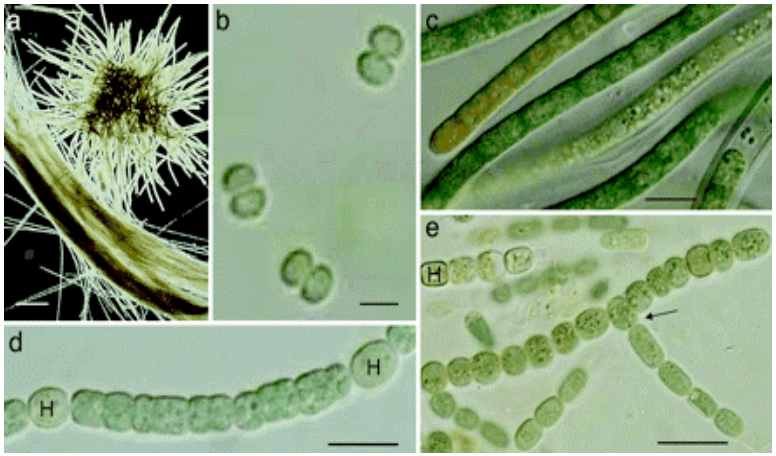

Cyanobacterial strains from 5 morphological sections

- Cyanobacteria are ubiquitous in terrestrial and freshwater, brackish, and marine environments, and in food, with widespread human exposure, both nationally and internationally
- Water pollution, eutrophication, and global warming trigger algal blooms (geographic dispersion), population density
- Cyanotoxin produced by cyanobacteria a growing concern for human health, recreation, and water-based industries
- Cyanotoxin production has wide but irregular occurrence phylogenetically

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PNAS

Proceedings of the National Academy of Sciences April 2005

Diverse taxa of cyanobacteria produce ß-*N*-methylamino-L-alanine, a neurotoxic amino acid

Cox et al.

- **Single neurotoxin, ß-*N*-methylamino-L-alanine (BMAA), produced by all known groups of cyanobacteria (symbiots and free-living)**
- **BMAA implicated as possible cause of ALS/Parkinsonism-dementia complex with an extremely high rate among Chamorro people of Guam**
- **BMAA detected in brain tissues in Canadian Alzheimer's patients, and in cyanobacterial culture samples worldwide**
- **BMAA produced in all members of free-living cyanobacterial sections, in 97% of strains tested, and in bloom-forming cyanobacteria from Baltic Sea**

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SCIENTIFIC AMERICAN

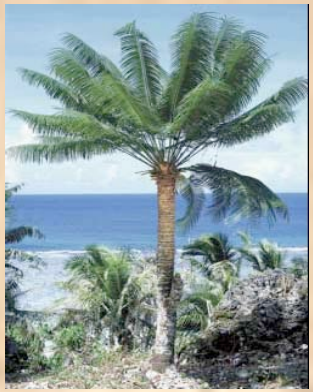
June 2005

Brain-Destroying Algae?

JAMA®

The Journal of the American Medical Association May 2005

Environmental Neurotoxin May Pose a Health Threat



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Hurricane Katrina
August 29, 2005

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CDC and EPA Activities

Department of Health and Human Services
Centers for Disease Control and Prevention

Environmental Health Needs and Habitability Assessment

Joint Taskforce
Centers for Disease Control and Prevention
U.S. Environmental Protection Agency

Hurricane Katrina Response

September 17, 2005

Information about other activities:

http//www.cdc.gov http://www.epa.gov

CDC-EPA task force established by DHHS to provide an initial assessment of the overarching environmental health and infrastructure issues faced by New Orleans to reinhabit the city:

Drinking water

Wastewater

Solid waste/debris

Sediments/soil contamination (toxic chemicals)

Power

Natural gas

Housing

Unwatering/flood water

Occupational safety and public security

Vector/rodent/animal control

Road conditions

Underground storage tanks (gasoline)

Food safety

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News Release

September 13, 2005

NIEHS Awards $37 Million to Train Emergency and Hazardous Waste Workers

- More than $37 million will go to workers involved in emergency response and hazardous waste clean-up
- Grants provide training designed to protect workers and their communities from exposure to toxic materials encountered during hazardous waste operations and chemical emergency response
- Award programs:
  - Hazmat Disaster Preparedness Training Program
  - Hazardous Waste Worker Training Program
  - DOE Nuclear Weapons Cleanup Training Program
  - Minority Worker Training Program

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Institute of Medicine
The National Academies of Science

Advisors to the Nation on Science, Engineering, and Medicine

EHSRT
INSTITUTE OF MEDICINE
THE NATIONAL ACADEMIES
Roundtable on Environmental Health Sciences, Research, and Medicine

Environmental Public Health Impacts of Disasters: Hurricane Katrina

Sponsored by

The Roundtable on Environmental Health Sciences, Research, and Medicine

Washington, D.C. 20004

October 20, 2005

- **One in a series of IOM workshops on environmental exposures and effects on human health during recovery**
- **Highlight the need for a coordinated environmental health effort**
- **Focus on:**
  - Issues of rapid assessment and identification of environmentally-related diseases
  - Impact of exposures on vulnerable populations
  - Social and ethical issues and community involvement
  - Research tools that need to be developed for monitoring exposure and health

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Vision for NIEHS

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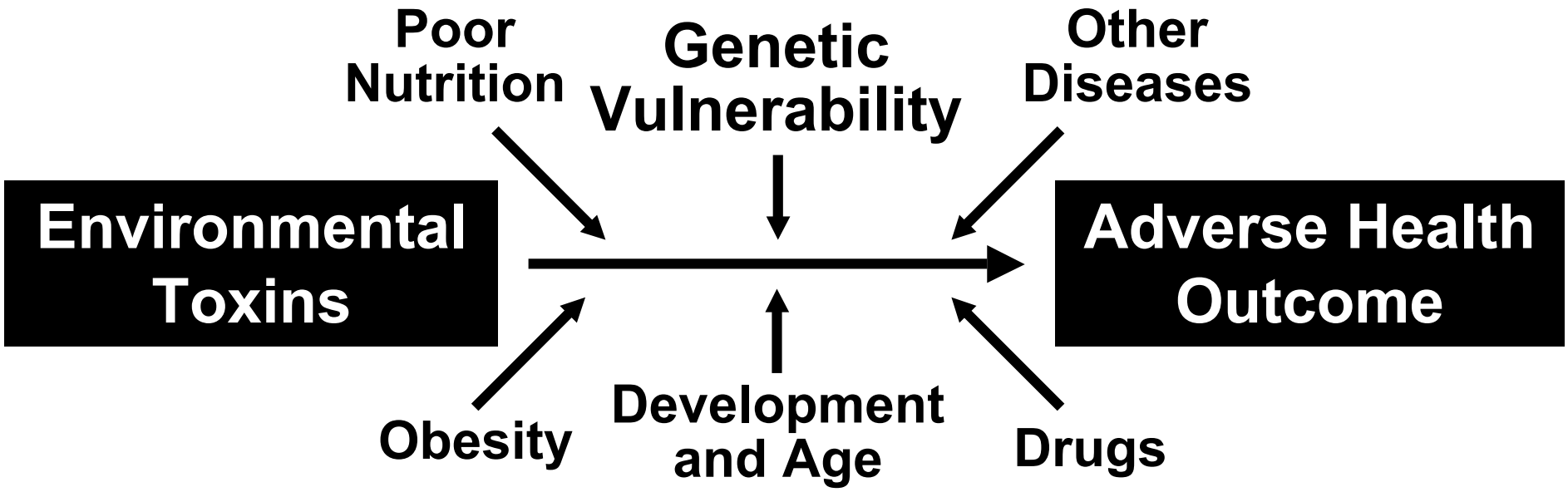
Why do certain people develop disease when challenged with an environmental toxin while others remain healthy?



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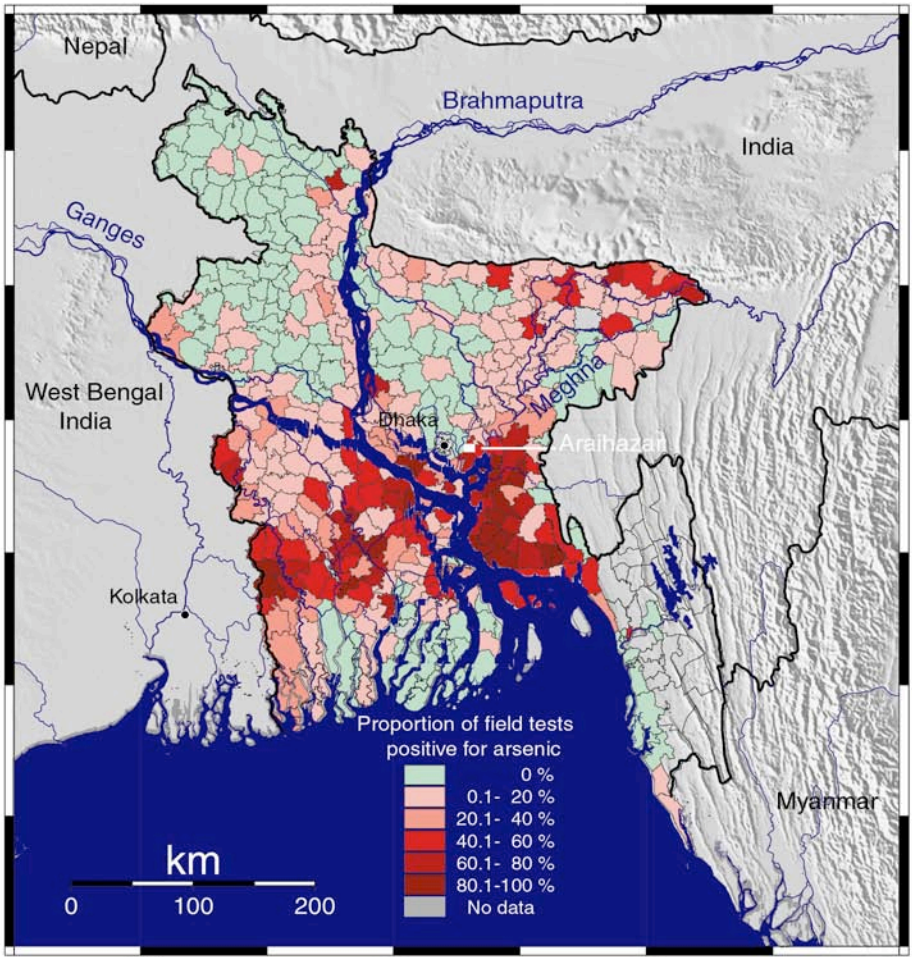
Scientific Orientation: Global Environmental Health



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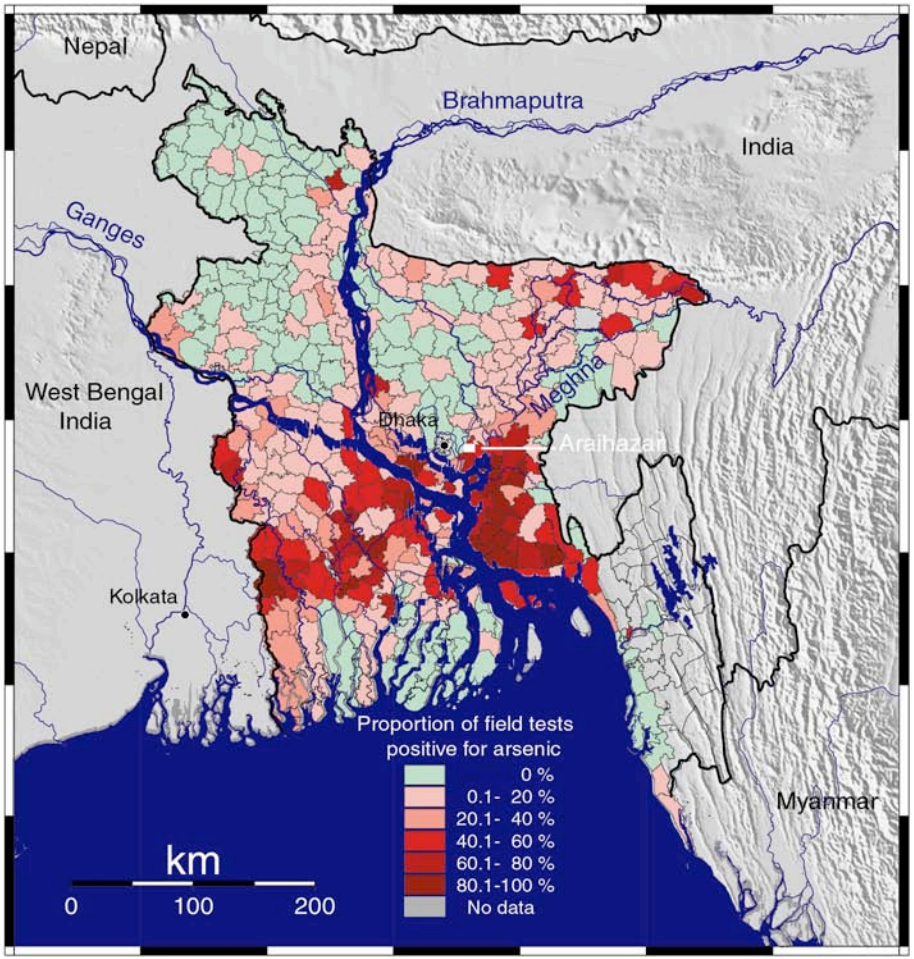
Scientific Orientation: Global Environmental Health



- Impact of environmental toxicants can be far-reaching; crossing all borders
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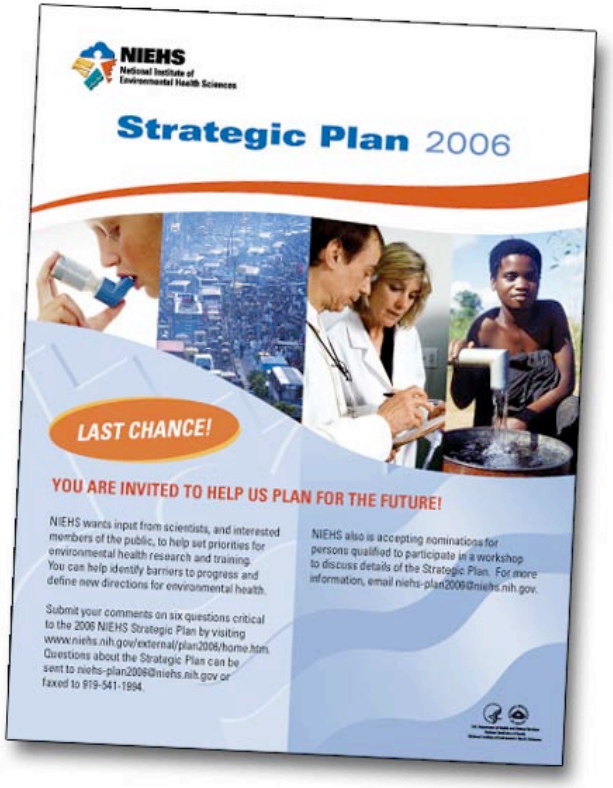
Developing a Strategic Plan



- **Federal register and NIEHS website**
  www.niehs.nih.gov/external/plan2006/home.htm
- **Strategic Planning Forum in October 2005**
- **Draft document available for public comment**
- **Final document released in early 2006**

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Ensuring a Transparent Process: Town Meetings and Website

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Providing Some Perspective

- **Scientific vision and need for change**
- **Strategic planning**
- **Training**
- **Global environmental health**

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Figure D.1a
Distribution of NIEHS Research Center Awards
Within Centers Budget Line
(Dollars in Thousands)

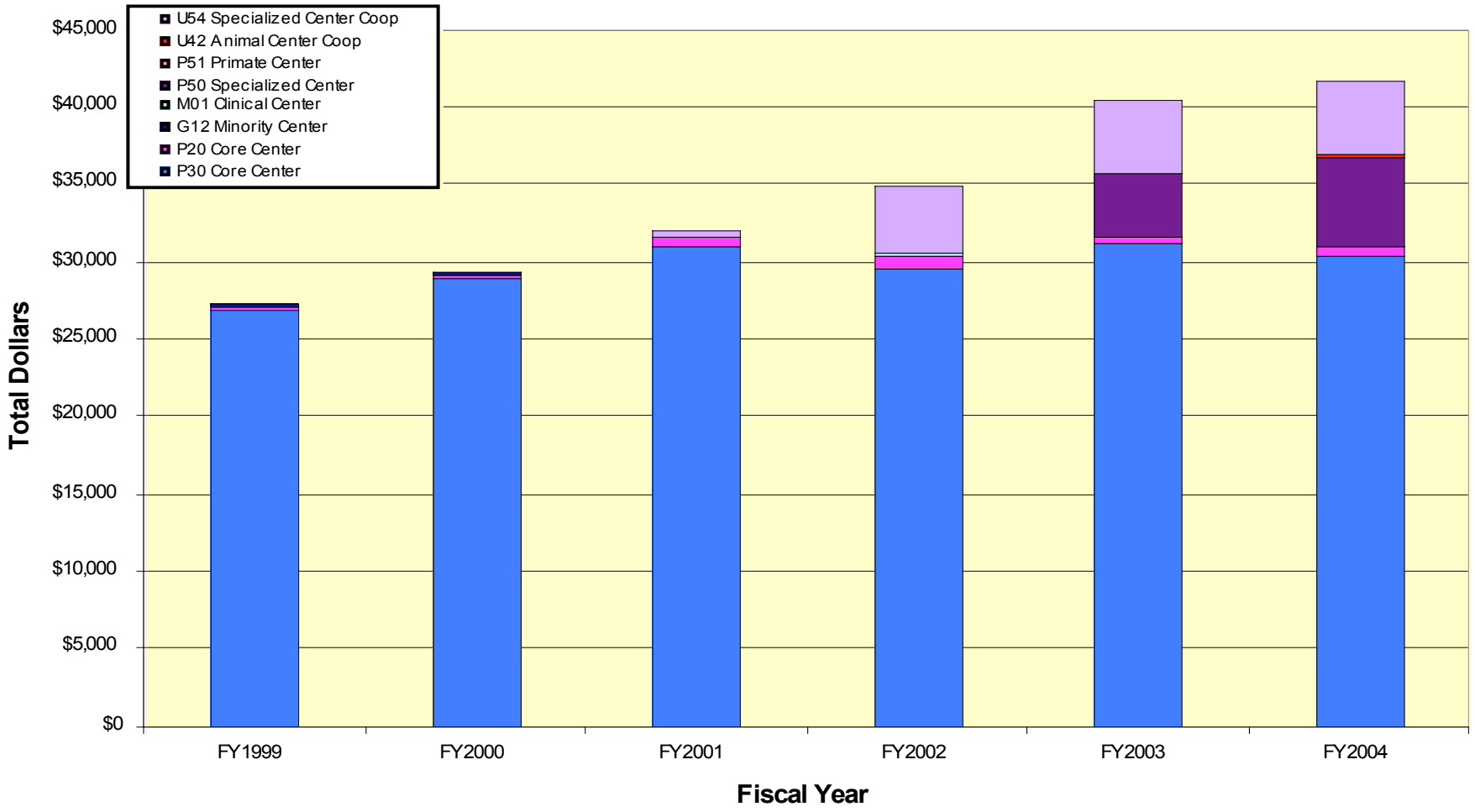

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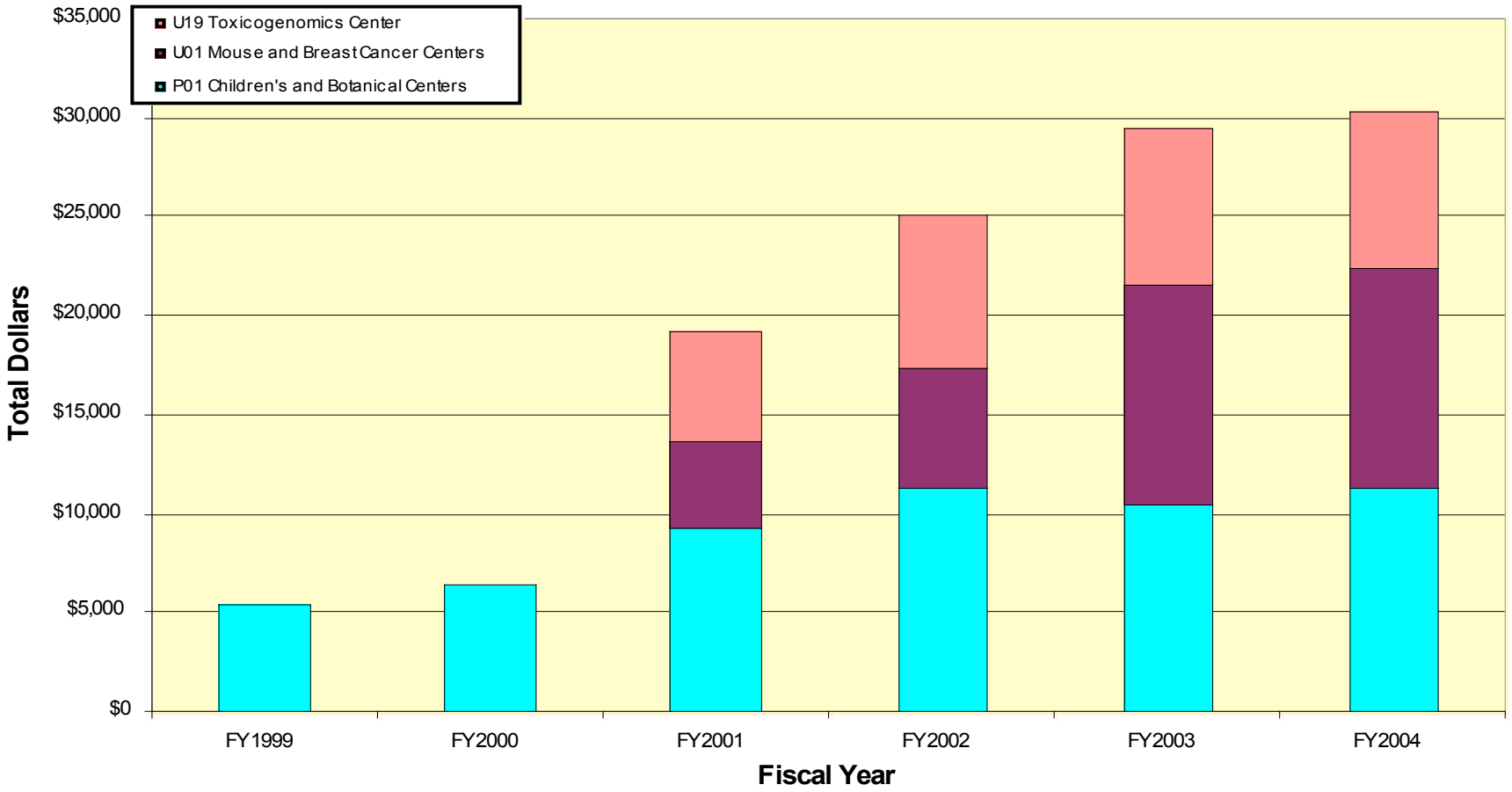
Figure D.1b
Distribution of NIEHS Research Center Awards
Outside of Centers Budget Line
(Dollars in Thousands)



Includes only Children's (P01), Botanical (P01), Mouse (U01), Breast Cancer (U01), and Toxicogenomics (U19) Centers
No other P01s, U01s, or U19s are included

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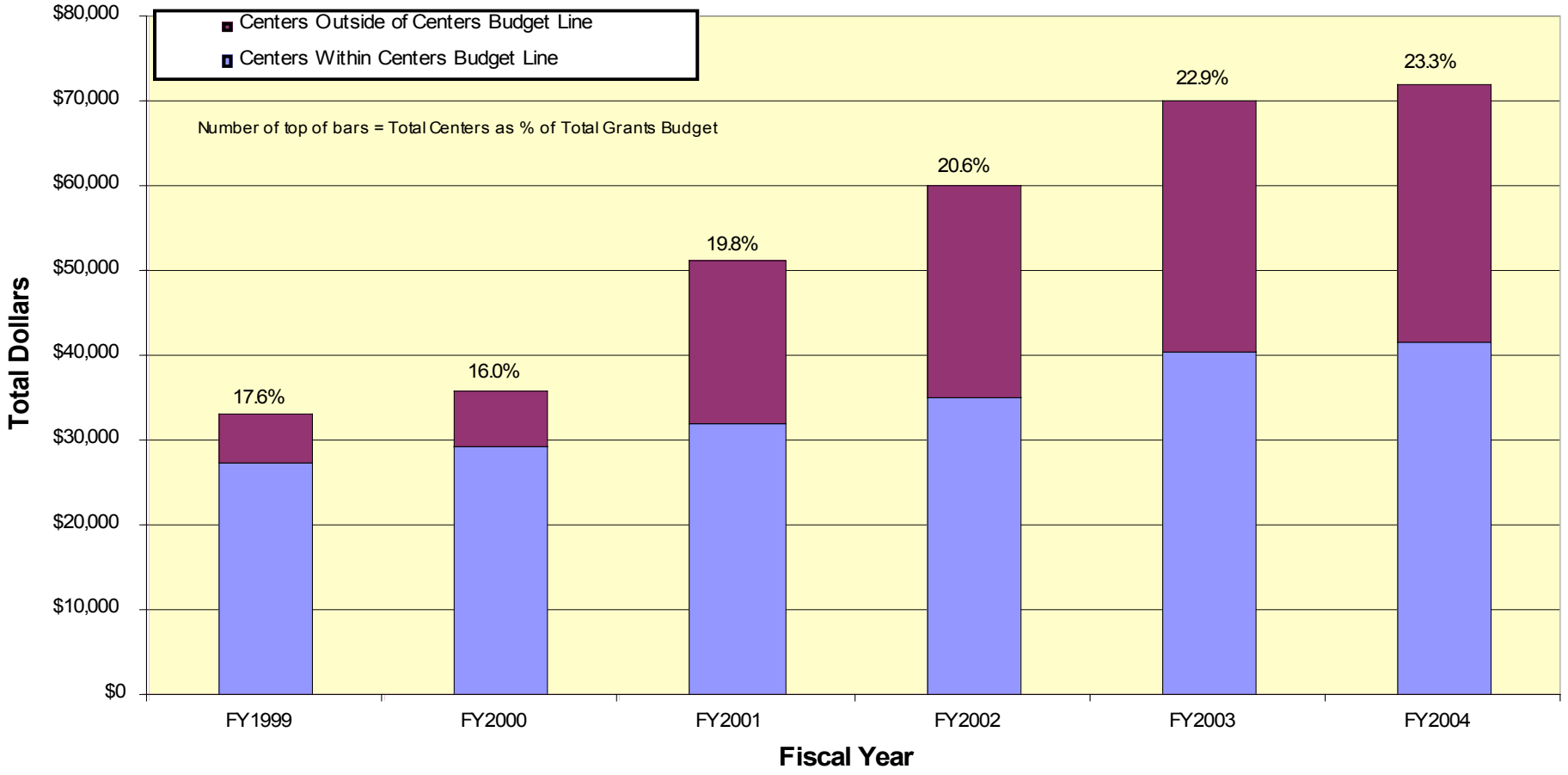
Figure D.1c
Distribution of NIEHS Research Center Awards
Within and Outside of Centers Budget Line
(Dollars in Thousands)



Centers Within Budget Line include P20 & P30 Core, G12 Minority, M01 Clinical, P50 Specialized, P51 Primate, U42 Animal, and U54 Specialized Centers
Centers Outside of Budget Line include P01 Children's and Botanical, U01 Mouse and Breast Cancer, and U19 Toxicogenomics Centers

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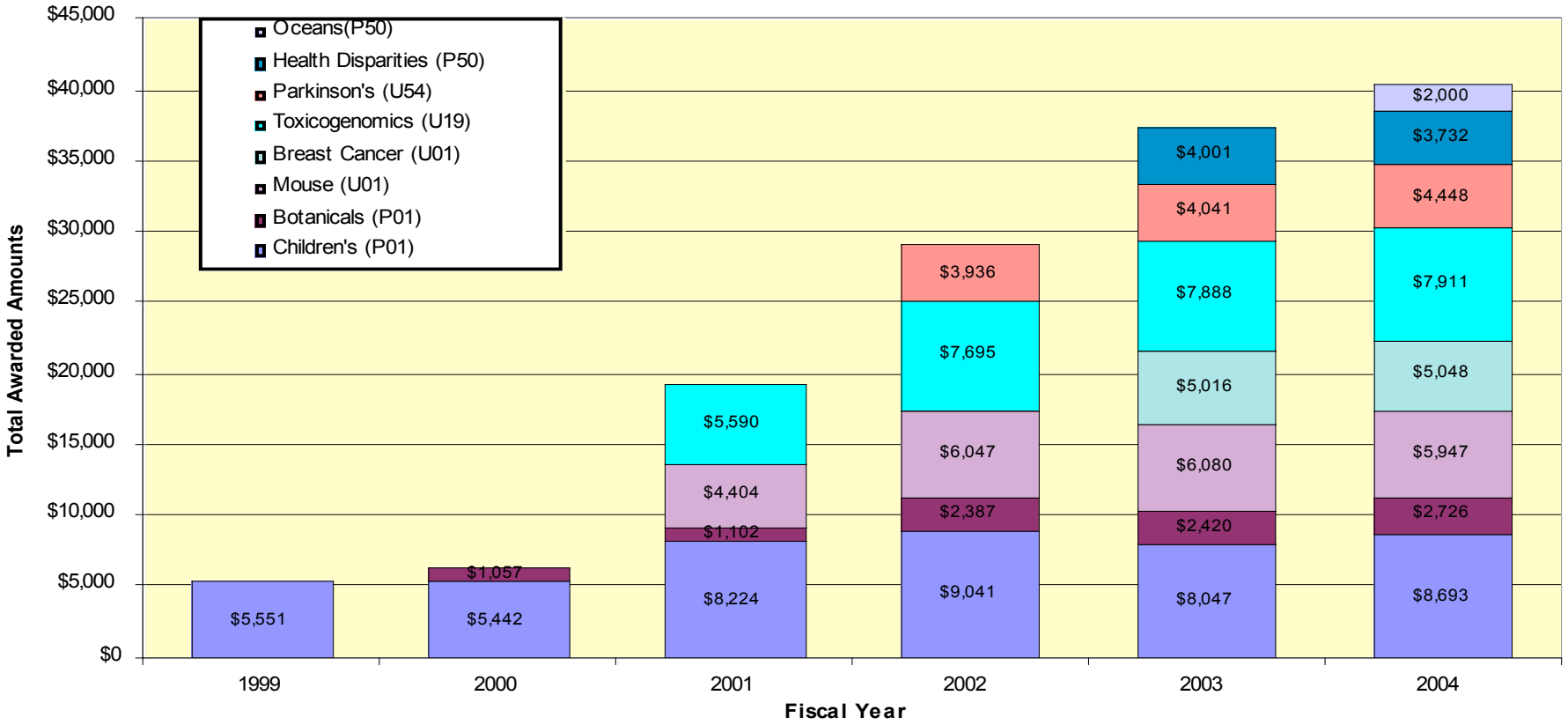
Figure D.1e
Distribution of NIEHS Research Center Awards
by Program Area Excluding Core Centers (P20 and P30)
(Dollars in Thousands)



Co-funding from NIH ODS for Botanical Centers: $1 million
Co-funding from NCI for Breast Cancer Centers: $2 million
Co-funding from NCI for Centers for Population Health and Health Disparities: $200,000

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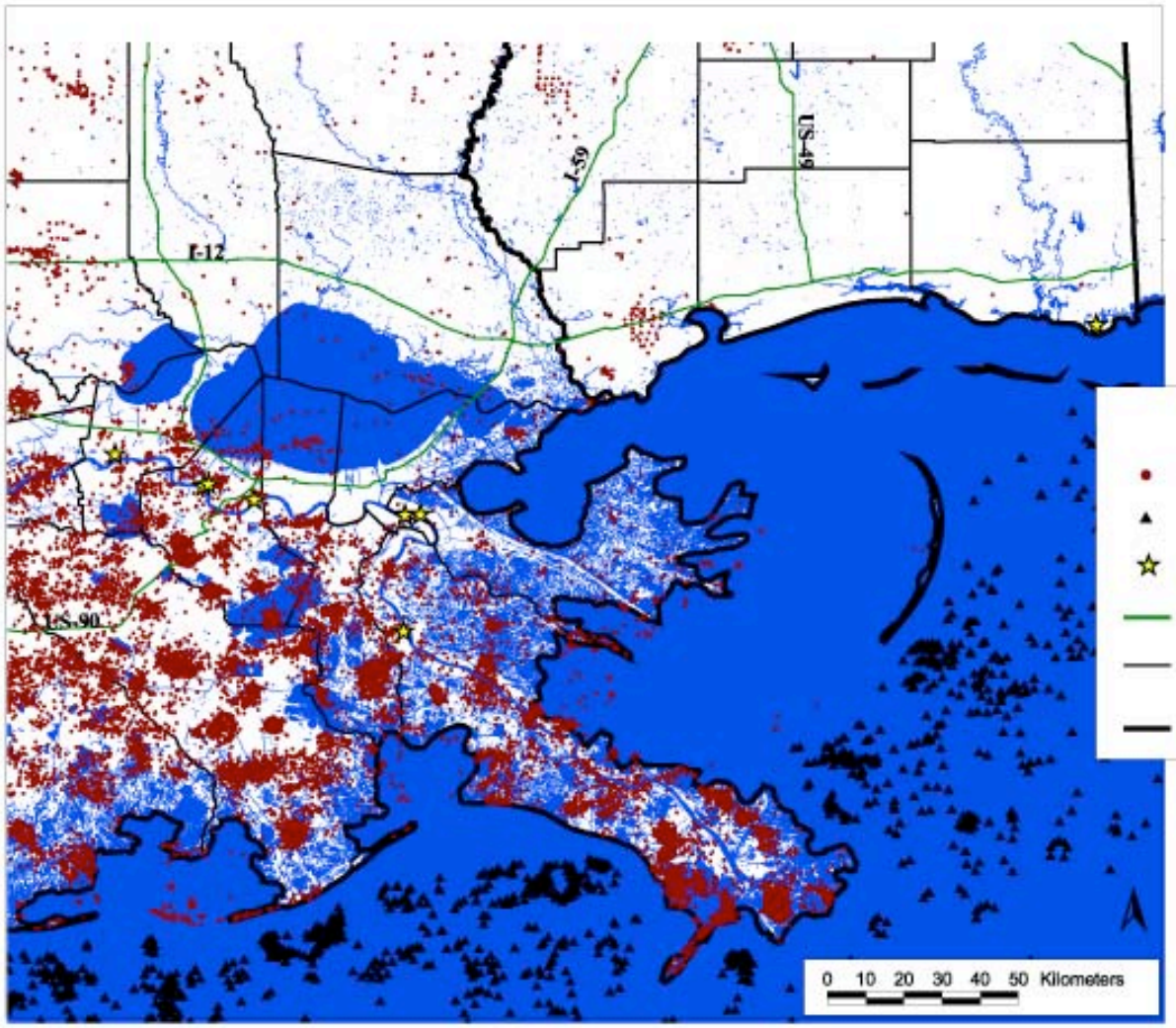
http://www-apps.niehs.nih.gov/katrina/



Superfund

- Duke
- UCSD

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Future Opportunities in Environmental Genomics

- Epigenetics
- Comparative Genomics
- Specialized Centers of Excellence
- Exposure Biology Initiative
- Enhance collaboration on cohort populations (NHGRI and NICHD) and case-control studies
- Support young investigators
  - Restructure training programs
  - ONES Program

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NIEHS Response to Hurricane Katrina

- Support medical NIH medical relief effort
- Website (www-apps.niehs.nih.gov/katrina/)
- Planned cooperative research with CDC and EPA
- Extramural research opportunities

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Workforce: Support scientists who will have the greatest impact on human health

US INSTITUTIONS

Institution (by rank)	Type of Institution	Postdocs in Life Sciences	Annual Postdoc Salary	Postdoc Office, Assoc., or Advisor?
1. US Environmental Protection Agency *Research Triangle Park, NC*	Government	25	$41,772–$60,576	Yes
2. Fred Hutchinson Cancer Research Center *Seattle, WA*	Private	286	$35,568–$51,036	Yes
3. National Cancer Institute *Bethesda/Frederick, MD*	Government	900–1000	$39,300–$58,400	Yes
4. National Institute of Environmental Health Sciences *Research Triangle Park, NC*	Government	240	$39,000–$65,000	Yes
5. Trudeau Institute *Saranac Lake, NY*	Private	28	$34,000–$41,000	No
6. University of North Carolina *Chapel Hill, NC*	Academic	483	mean: $38,568	Yes
7. Wadsworth Center	Government	75	mean: $36,000	Yes

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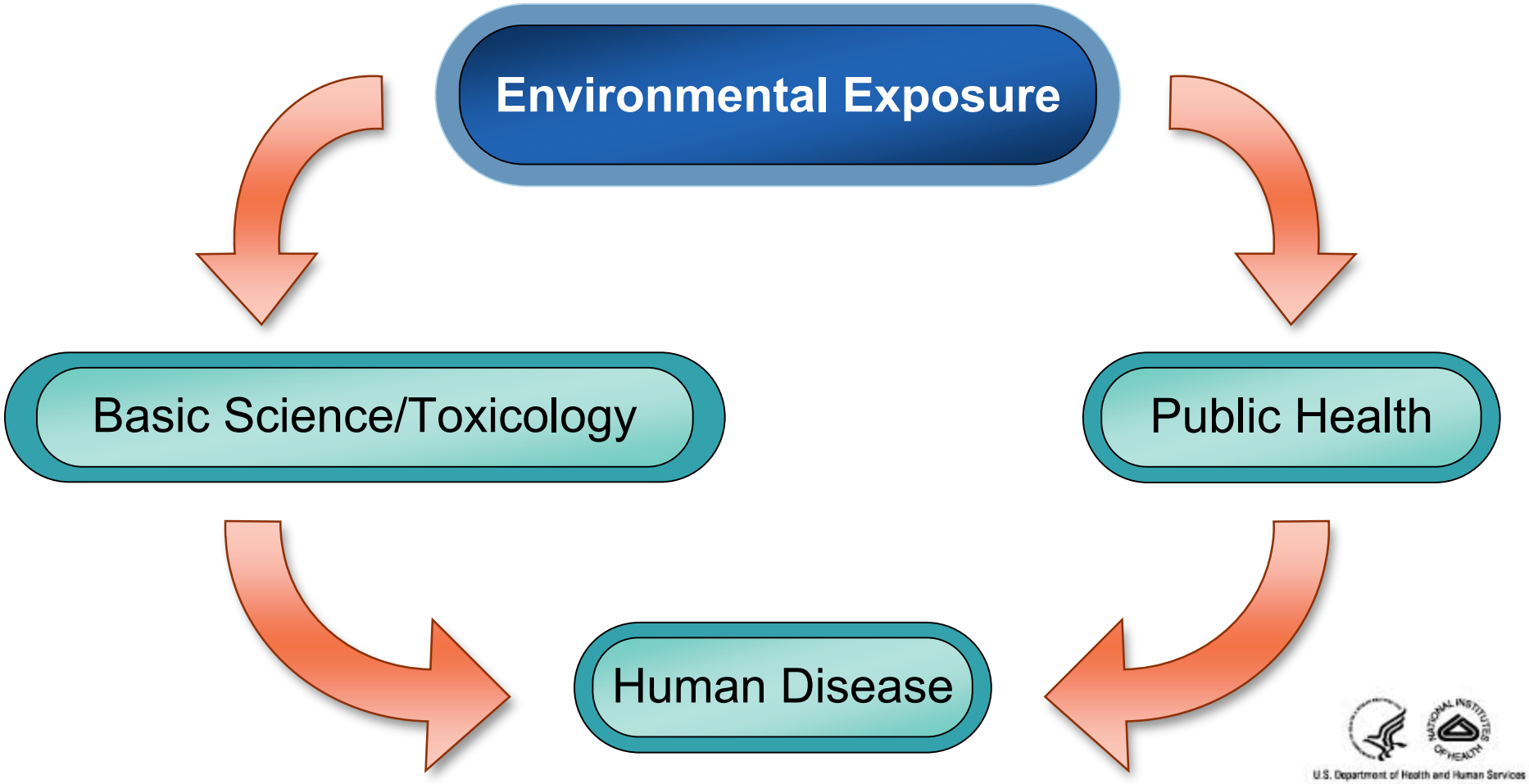
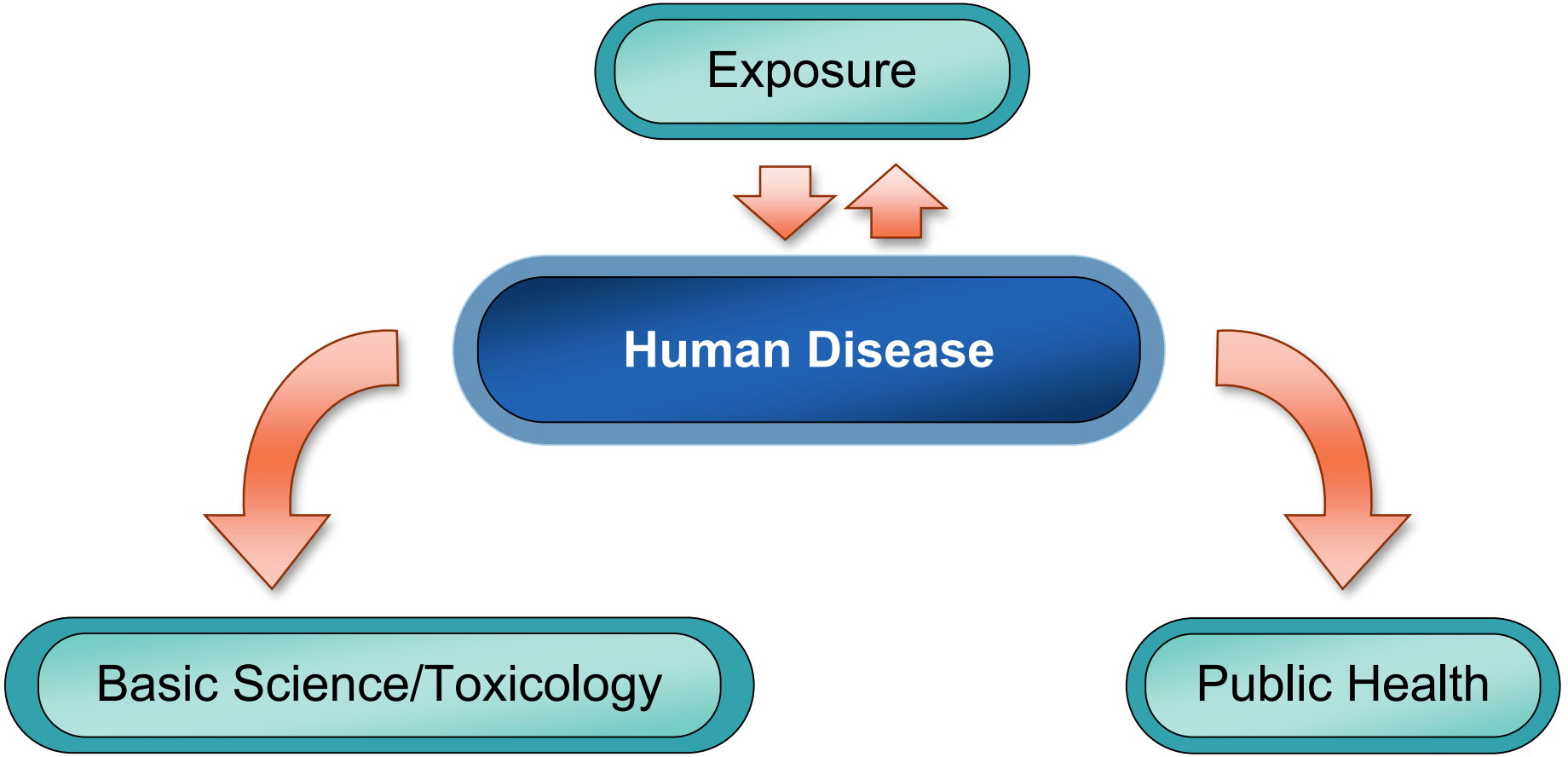
Shifting Our Emphasis: Traditional Approach



Shifting Our Emphasis: New Approach



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Cooperative Research with CDC and EPA